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RELATED PCT APPLICATION NUMBER: *PCT/US03/06793*

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Rita H. Jennings

Sir

Transmitted herewith for filing is a **PROVISIONAL** Patent Application under 37 C.F.R. §1.53(c) of:

	Attorney Dkt. No. 38205-P3002		Type a (+) in this box →	+
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For: **QUINAZOLINONE MODULATORS OF NUCLEAR RECEPTORS**

The subject matter in this application was not made under contract with an agency of the United States Government.

PROVISIONAL APPLICATION
DOCKET NO. 38205-P3002
Martin *et al.*

Enclosed are:

[X] The specification containing 273 pages including claims, abstract, and 20 Sheets of Figures (Figures 1, 2 and 3).

Status as Small Entity
[X] is claimed, reducing Filing Fee by one-half to $ 80.00
[ ] is not claimed.

[X] A check in the amount of $80.00 to cover the filing fee.

[ ] Charge $ to Deposit Account No. 50-1213.

[X] The Commissioner is hereby authorized to charge any fees, including any due herein, that may be required in this application during its entire pendency, or credit any overpayment, to Deposit Account No. 50-1213. If proper payment is not enclosed, such as a check in the wrong amount, unsigned, post-dated, otherwise improper or informal, or absent, the Commissioner is authorized to charge the unpaid amount or total amount due to Deposit Account No. 50-1213 during the entire pendency of this application. This sheet is filed in triplicate.

Respectfully submitted,
HELLER EHRMAN WHITE & McAULIFFE LLP

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QUINAZOLINONE MODULATORS OF NUCLEAR RECEPTORS

FIELD OF THE INVENTION

Quinazolinones, compositions containing quinazolinones and methods for modulating the activity of nuclear receptors using quinazolinones are provided. In particular, quinazolinones are provided for modulating the activity of FXR and orphan nuclear receptors.

BACKGROUND OF THE INVENTION

Nuclear Receptors

Nuclear receptors are a superfamily of regulatory proteins that are structurally and functionally related and are receptors for, *e.g.*, steroids, retinoids, vitamin D and thyroid hormones (see, *e.g.*, Evans (1988) *Science 240*:889-895). These proteins bind to cis-acting elements in the promoters of their target genes and modulate gene expression in response to ligands for the receptors.

Nuclear receptors can be classified based on their DNA binding properties (see, *e.g.*, Evans, *supra* and Glass (1994) *Endocr. Rev. 15*:391-407). For example, one class of nuclear receptors includes the glucocorticoid, estrogen, androgen, progestin and mineralocorticoid receptors which bind as homodimers to hormone response elements (HREs) organized as inverted repeats (see, *e.g.*, Glass, *supra*). A second class of receptors, including those activated by retinoic acid, thyroid hormone, vitamin D_3, fatty acids/peroxisome proliferators (*i.e.*, peroxisome proliferator activated receptor (PPAR)) and ecdysone, bind to HREs as heterodimers with a common partner, the retinoid X receptors (*i.e.*, RXRs, also known as the 9-*cis* retinoic acid receptors; see, *e.g.*, Levin *et al.* (1992) *Nature 355*:359-361 and Heyman *et al.* (1992) *Cell 68*:397-406).

RXRs are unique among the nuclear receptors in that they bind DNA as a homodimer and are required as a heterodimeric partner for a number of additional nuclear receptors to bind DNA (see, *e.g.*, Mangelsdorf *et al.* (1995) *Cell 83*:841-850). The latter receptors, termed

the class II nuclear receptor subfamily, include many which are established or implicated as important regulators of gene expression. There are three RXR genes (see, *e.g.*, Mangelsdorf *et al.* (1992) *Genes Dev. 6*:329-344), coding for RXRα, -β, and -γ, all of which are able to heterodimerize with any of the class II receptors, although there appear to be preferences for distinct RXR subtypes by partner receptors *in vivo* (see, *e.g.*, Chiba *et al.* (1997) *Mol. Cell. Biol. 17*:3013-3020). In the adult liver, RXRα is the most abundant of the three RXRs (see, *e.g.*, Mangelsdorf *et al.* (1992) *Genes Dev. 6*:329-344), suggesting that it might have a prominent role in hepatic functions that involve regulation by class II nuclear receptors. See also, Wan *et al.* (2000) *Mol. Cell. Biol. 20*:4436-4444.

Orphan Nuclear Receptors

Included in the nuclear receptor superfamily of regulatory proteins are nuclear receptors for whom the ligand is known and those which lack known ligands. Nuclear receptors falling in the latter category are referred to as orphan nuclear receptors. The search for activators for orphan receptors has led to the discovery of previously unknown signaling pathways (see, *e.g.*, Levin *et al.*, (1992), *supra* and Heyman *et al.*, (1992), *supra*). For example, it has been reported that bile acids, which are involved in physiological processes such as cholesterol catabolism, are ligands for FXR (*infra*).

Since it is known that products of intermediary metabolism act as transcriptional regulators in bacteria and yeast, such molecules may serve similar functions in higher organisms (see, *e.g.*, Tomkins (1975) *Science 189*:760-763 and O'Malley (1989) *Endocrinology 125*:1119-1120). For example, one biosynthetic pathway in higher eukaryotes is the mevalonate pathway, which leads to the synthesis of cholesterol, bile acids, porphyrin, dolichol, ubiquinone, carotenoids, retinoids, vitamin D, steroid hormones and farnesylated proteins.

FXR

FXR (originally isolated as RIP14 (retinoid X receptor-interacting protein-14), see, *e.g.*, Seol *et al.* (1995) *Mol. Endocrinol. 9*:72-85) is a member of the nuclear hormone receptor superfamily and is primarily expressed in the liver, kidney and intestine (see, *e.g.*, Seol *et al.*, *supra* and Forman *et al.* (1995) *Cell 81*:687-693). It functions as a heterodimer with the retinoid X receptor (RXR) and binds to response elements in the promoters of target genes to regulate gene transcription. The FXR-RXR heterodimer binds with highest affinity to an inverted repeat-1 (IR-1) response element, in which consensus receptor-binding hexamers are separated by one nucleotide. FXR is part of an interrelated process, in that FXR is activated by bile acids (the end product of cholesterol metabolism) (see, *e.g.*, Makishima *et al.* (1999) *Science 284*:1362-1365, Parks *et al.* (1999) *Science 284*:1365-1368, Wang *et al.* (1999) *Mol. Cell. 3*:543-553), which serve to inhibit cholesterol catabolism. See also, Urizar *et al.* (2000) *J. Biol. Chem. 275*:39313-39317.

Nuclear Receptors and Disease

Nuclear receptor activity has been implicated in a variety of diseases and disorders, including, but not limited to, hypercholesterolemia (see, *e.g.*, International Patent Application Publication No. WO 00/57915), osteoporosis and vitamin deficiency (see, *e.g.*, U.S. Patent No. 6,316,5103), hyperlipoproteinemia (see, *e.g.*, International Patent Application Publication No. WO 01/60818), hypertriglyceridemia, lipodystrophy, peripheral occlusive disease, ischemic stroke, hyperglycemia and diabetes mellitus (see, *e.g.*, International Patent Application Publication No. WO 01/82917), atherosclerosis and gallstones (see, *e.g.*, International Patent Application Publication No. WO 00/37077), disorders of the skin and mucous membranes (see, *e.g.*, U.S. Patent Nos. 6,184,215 and 6,187,814, and International Patent Application Publication No. WO 98/32444), acne (see, *e.g.*, International

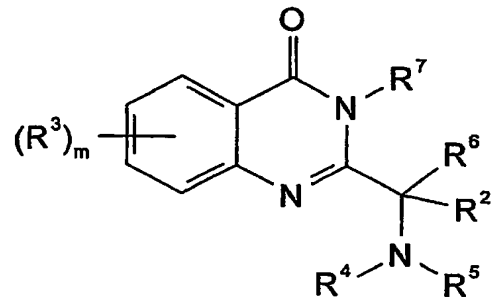
Patent Application Publication No. WO 00/49992), and cancer, Parkinson's disease and Alzheimer's disease (see, *e.g.*, International Patent Application Publication No. WO 00/17334). Activity of nuclear receptors, including FXR and/or orphan nuclear receptors, has been implicated in physiological processes including, but not limited to, bile acid biosynthesis, cholesterol metabolism or catabolism, and modulation of cholesterol 7α-hydroxylase gene (CYP7A1) transcription (see, *e.g.*, Chiang *et al.* (2000) *J. Biol. Chem. 275*:10918-10924), HDL metabolism (see, *e.g.*, Urizar *et al.* (2000) *J. Biol. Chem. 275*:39313-39317), hyperlipidemia, cholestasis, and increased cholesterol efflux and increased expression of ATP binding cassette transporter protein (ABC1) (see, *e.g.*, International Patent Application Publication No. WO 00/78972).

Thus, there is a need for compounds, compositions and methods of modulating the activity of nuclear receptors, including FXR and/or orphan nuclear receptors. Such compounds are useful in the treatment, prevention, or amelioration of one or more symptoms of diseases or disorders in which nuclear receptor activity is implicated.

SUMMARY OF THE INVENTION

Compounds for use in compositions and methods for modulating the activity of nuclear receptors are provided. In particular, compounds for use in compositions and methods for modulating farnesoid X receptor (FXR) and/or orphan nuclear receptors, are provided. In certain embodiments, the compounds are quinazolinones. In one embodiment, the compounds provided herein are agonists of FXR. In another embodiment, the compounds provided herein are antagonists of FXR. Agonists that exhibit low efficacy are, in certain embodiments, antagonists.

In one embodiment, the compounds for use in the compositions and methods provided herein have formula I:



wherein:

R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{91} or $NR^{92}R^{93}$, with the proviso that R^7 is not 4-(1,1,1,3,3,3-hexafluoro-2-hydroxy-2-propyl)phenyl;

R^{91} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{92} and R^{93} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_jR^{94}$ where j is 1 or 2, and $C(M)R^{95}$, where M is

selected from O and S; or R^{92} and R^{93} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{94} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{95} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{96} or $NR^{97}R^{98}$; R^{96} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{97} and R^{98} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

each R^3 is selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or

unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2; or any two R^3 groups, which substitute adjacent carbons on the ring, together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkylenedioxy, substituted or unsubstituted thioalkylenoxy, or substituted or unsubstituted alkylenedithioxy;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $C(D)R^{15}$ where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl,

aralkyl and heteroaralkyl, or R^{18} and R^{19} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or $C(D)R^{15}$ where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{12} or $NR^{10}R^{11}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl; or (ii) R^2 and R^6 together form substituted or unsubstituted alkylene or substituted or unsubstituted alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or

unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted

heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted

aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or

unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 4, 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^2-R^7, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl,

triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^{+}R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or

alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy (*i.e.*, -O-$(CH_2)_y$-O-), thioalkylenoxy (*i.e.*, -S-$(CH_2)_y$-O-) or alkylenedithioxy (*i.e.*, -S-$(CH_2)_y$-S-) where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -$NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -$NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy,

aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy (*i.e.*, $-O-(CH_2)_y-O-$), thioalkylenoxy (*i.e.*, $-S-(CH_2)_y-O-$) or alkylenedithioxy (*i.e.*, $-S-(CH_2)_y-S-$) where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene.

In one embodiment, R^7 is substituted or unsubstituted phenyl, and is selected with the proviso that it is not substituted at the 4-position with $-C(OH)(CF_3)_2$.

The groups R^2, R^3, R^4, R^5 and R^7 are selected such that the resulting compound has nuclear receptor modulation activity, such as in at least one assay described herein, such as FXR antagonist or agonist activity, and, in certain embodiments, at an IC_{50} or EC_{50} of less than about 100 μM. The FXR IC_{50} or EC_{50} values for the compounds provided herein are, in certain embodiments, less than about 50 μM, 25 μM, 10 μM, 1 μM, 100 nM, 10 nM or 1 nM.

Also of interest are any pharmaceutically-acceptable derivatives, including salts, esters, enol ethers, enol esters, solvates, hydrates and prodrugs of the compounds described herein. Pharmaceutically-acceptable salts, include, but are not limited to, amine salts, such as but not limited to N,N'-dibenzylethylenediamine, chloroprocaine, choline, ammonia, diethanolamine and other hydroxyalkylamines, ethylenediamine, N-methylglucamine, procaine, N-benzylphenethylamine, 1-para-chlorobenzyl-2-pyrrolidin-1'-ylmethylbenzimidazole, diethylamine and other alkylamines, piperazine and tris(hydroxymethyl)aminomethane; alkali metal salts, such as but not limited to lithium, potassium and sodium; alkali earth metal salts, such as but not limited to barium, calcium and magnesium; transition metal salts, such as but not limited to zinc, aluminum, and other metal salts, such as but not limited to sodium hydrogen phosphate and disodium phosphate; and also including, but not limited to, salts of mineral acids, such as but not limited to hydrochlorides and sulfates; and salts of organic acids, such as but not limited to acetates, lactates, malates, tartrates, citrates, ascorbates, succinates, butyrates, valerates and fumarates.

Pharmaceutical compositions formulated for administration by an appropriate route and means containing effective concentrations of one or more of the compounds provided herein, or pharmaceutically acceptable derivatives thereof, that deliver amounts effective for the treatment, prevention, or amelioration of one or more symptoms of diseases or disorders that are modulated or otherwise affected by nuclear receptor

activity, including FXR and/or orphan nuclear receptor activity, or in which nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, is implicated, are also provided. The effective amounts and concentrations are effective for ameliorating any of the symptoms of any of the diseases or disorders.

Methods for treatment, prevention, or amelioration of one or more symptoms of diseases or disorders mediated by or in which nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, is implicated, are provided. Such methods include methods of treatment, prevention and amelioration of one or more symptoms of hypercholesterolemia, hyperlipoproteinemia, hypertriglyceridemia, lipodystrophy, hyperglycemia, diabetes mellitus, dyslipidemia, atherosclerosis, gallstone disease, acne vulgaris, acneiform skin conditions, diabetes, Parkinson's disease, cancer, Alzheimer's disease, inflammation, immunological disorders, lipid disorders, obesity, conditions characterized by a perturbed epidermal barrier function, hyperlipidemia, cholestasis, peripheral occlusive disease, ischemic stroke, conditions of disturbed differentiation or excess proliferation of the epidermis or mucous membrane, or cardiovascular disorders, using one or more of the compounds provided herein, or pharmaceutically acceptable derivatives thereof.

Methods of modulating the activity of nuclear receptors, including FXR and/or orphan nuclear receptors, using the compounds and compositions provided herein are also provided. The compounds and compositions provided herein are active in assays that measure the activity of nuclear receptors, including FXR and/or orphan nuclear receptors, including the assays provided herein. These methods include inhibiting and up-regulating the activity of nuclear receptors, including FXR and/or orphan nuclear receptors.

Methods of reducing cholesterol levels in a subject in need thereof by administration of one or more compounds or compositions provided herein are also provided.

Methods of modulating cholesterol metabolism using the compounds and compositions provided herein are provided.

Methods of treating, preventing, or ameliorating one or more symptoms of diseases or disorders which are affected by cholesterol, triglyceride, or bile acid levels by administration of one or more of the compounds and compositions provided herein are also provided.

In practicing the methods, effective amounts of the compounds or compositions containing therapeutically effective concentrations of the compounds, which are formulated for systemic delivery, including parenteral, oral, or intravenous delivery, or for local or topical application, for the treatment of nuclear receptor, including FXR and/or orphan nuclear receptor, mediated diseases or disorders, or diseases or disorders in which nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, is implicated, including, but not limited to, hypercholesterolemia, hyperlipoproteinemia, hypertriglyceridemia, lipodystrophy, hyperglycemia, diabetes mellitus, dyslipidemia, atherosclerosis, gallstone disease, acne vulgaris, acneiform skin conditions, diabetes, Parkinson's disease, cancer, Alzheimer's disease, inflammation, immunological disorders, lipid disorders, obesity, conditions characterized by a perturbed epidermal barrier function, hyperlipidemia, cholestasis, peripheral occlusive disease, ischemic stroke, conditions of disturbed differentiation or excess proliferation of the epidermis or mucous membrane, or cardiovascular disorders, are administered to an individual exhibiting the symptoms of these diseases or disorders. The amounts are effective to ameliorate or eliminate one or more symptoms of the diseases or disorders.

Articles of manufacture containing packaging material, a compound or composition, or pharmaceutically acceptable derivative thereof,

provided herein, which is effective for modulating the activity of nuclear receptors, including FXR and/or orphan nuclear receptors, or for treatment, prevention or amelioration of one or more symptoms of nuclear receptor, including FXR and/or orphan nuclear receptor, mediated diseases or disorders, or diseases or disorders in which nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, is implicated, within the packaging material, and a label that indicates that the compound or composition, or pharmaceutically acceptable derivative thereof, is used for modulating the activity of nuclear receptors, including FXR and/or orphan nuclear receptors, or for treatment, prevention or amelioration of one or more symptoms of nuclear receptor, including FXR and/or orphan nuclear receptor, mediated diseases or disorders, or diseases or disorders in which nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, is implicated, are provided.

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1, 2 and 3 provide the structures for exemplary compounds within the scope of those provided herein for use in the compositions and methods provided herein.

DETAILED DESCRIPTION OF EMBODIMENTS

A. Definitions

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of ordinary skill in the art to which this invention belongs. All patents, applications, published applications and other publications are incorporated by reference in their entirety. In the event that there are a plurality of definitions for a term herein, those in this section prevail unless stated otherwise.

As used herein, a nuclear receptor is a member of a superfamily of regulatory proteins that are receptors for, *e.g.*, steroids, retinoids, vitamin D and thyroid hormones. These proteins bind to cis-acting elements in the promoters of their target genes and modulate gene expression in

response to a ligand therefor. Nuclear receptors may be classified based on their DNA binding properties. For example, the glucocorticoid, estrogen, androgen, progestin and mineralocorticoid receptors bind as homodimers to hormone response elements (HREs) organized as inverted repeats. Another example are receptors, including those activated by retinoic acid, thyroid hormone, vitamin D_3, fatty acids/peroxisome proliferators and ecdysone, that bind to HREs as heterodimers with a common partner, the retinoid X receptor (RXR). Among the latter receptors are FXR.

As used herein, an orphan nuclear receptor is a nuclear receptor for which the natural ligand is unknown.

As used herein, farnesoid X receptor or FXR refers to a nuclear receptor as described in U.S. Patent No. 6,005,086.

As used herein, pharmaceutically acceptable derivatives of a compound include salts, esters, enol ethers, enol esters, acetals, ketals, orthoesters, hemiacetals, hemiketals, acids, bases, solvates, hydrates or prodrugs thereof. Such derivatives may be readily prepared by those of skill in this art using known methods for such derivatization. The compounds produced may be administered to animals or humans without substantial toxic effects and either are pharmaceutically active or are prodrugs. Pharmaceutically acceptable salts include, but are not limited to, amine salts, such as but not limited to N,N'-dibenzylethylenediamine, chloroprocaine, choline, ammonia, diethanolamine and other hydroxyalkylamines, ethylenediamine, N-methylglucamine, procaine, N-benzylphenethylamine, 1-para-chlorobenzyl-2-pyrrolidin-1'-ylmethyl-benzimidazole, diethylamine and other alkylamines, piperazine and tris(hydroxymethyl)aminomethane; alkali metal salts, such as but not limited to lithium, potassium and sodium; alkali earth metal salts, such as but not limited to barium, calcium and magnesium; transition metal salts, such as but not limited to zinc; and other metal salts, such as but not limited to sodium hydrogen phosphate and disodium phosphate; and also

including, but not limited to, salts of mineral acids, such as but not limited to hydrochlorides and sulfates; and salts of organic acids, such as but not limited to acetates, lactates, malates, tartrates, citrates, ascorbates, succinates, butyrates, valerates and fumarates.

Pharmaceutically acceptable esters include, but are not limited to, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, heteroaralkyl, cycloalkyl and heterocyclyl esters of acidic groups, including, but not limited to, carboxylic acids, phosphoric acids, phosphinic acids, sulfonic acids, sulfinic acids and boronic acids. Pharmaceutically acceptable enol ethers include, but are not limited to, derivatives of formula C=C(OR) where R is hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, heteroaralkyl, cycloalkyl ar heterocyclyl. Pharmaceutically acceptable enol esters include, but are not limited to, derivatives of formula C=C(OC(O)R) where R is hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, heteroaralkyl, cycloalkyl ar heterocyclyl. Pharmaceutically acceptable solvates and hydrates are complexes of a compound with one or more solvent or water molecules, or 1 to about 100, or 1 to about 10, or one to about 2, 3 or 4, solvent or water molecules.

As used herein, treatment means any manner in which one or more of the symptoms of a disease or disorder are ameliorated or otherwise beneficially altered. Treatment also encompasses any pharmaceutical use of the compositions herein, such as use for treating a nuclear receptor, including FXR and/or orphan nuclear receptor, mediated diseases or disorders, or diseases or disorders in which nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, is implicated.

As used herein, amelioration of the symptoms of a particular disorder by administration of a particular compound or pharmaceutical composition refers to any lessening, whether permanent or temporary, lasting or transient that can be attributed to or associated with administration of the composition.

As used herein, the IC_{50} refers to an amount, concentration or dosage of a particular test compound that achieves a 50% inhibition of a maximal response, such as modulation of FXR activity, in an assay that measures such response.

As used herein, EC_{50} refers to a dosage, concentration or amount of a particular test compound that elicits a dose-dependent response at 50% of maximal expression of a particular response that is induced, provoked or potentiated by the particular test compound.

As used herein, a prodrug is a compound that, upon *in vivo* administration, is metabolized by one or more steps or processes or otherwise converted to the biologically, pharmaceutically or therapeutically active form of the compound. To produce a prodrug, the pharmaceutically active compound is modified such that the active compound will be regenerated by metabolic processes. The prodrug may be designed to alter the metabolic stability or the transport characteristics of a drug, to mask side effects or toxicity, to improve the flavor of a drug or to alter other characteristics or properties of a drug. By virtue of knowledge of pharmacodynamic processes and drug metabolism *in vivo*, those of skill in this art, once a pharmaceutically active compound is known, can design prodrugs of the compound (see, *e.g.*, Nogrady (1985) *Medicinal Chemistry A Biochemical Approach*, Oxford University Press, New York, pages 388-392).

It is to be understood that the compounds provided herein may contain chiral centers. Such chiral centers may be of either the (R) or (S) configuration, or may be a mixture thereof. Thus, the compounds provided herein may be enantiomerically pure, or be stereoisomeric or diastereomeric mixtures. In the case of amino acid residues, such residues may be of either the L- or D-form. The configuration for naturally occurring amino acid residues is generally L. When not specified the residue is the L form. As used herein, the term "amino acid" refers to α-amino acids which are racemic, or of either the D- or L-configuration.

The designation "d" preceding an amino acid designation (*e.g.*, dAla, dSer, dVal, etc.) refers to the D-isomer of the amino acid. The designation "dl" preceding an amino acid designation (*e.g.*, dlPip) refers to a mixture of the L- and D-isomers of the amino acid. It is to be understood that the chiral centers of the compounds provided herein may undergo epimerization *in vivo*. As such, one of skill in the art will recognize that administration of a compound in its (R) form is equivalent, for compounds that undergo epimerization *in vivo*, to administration of the compound in its (S) form.

As used herein, substantially pure means sufficiently homogeneous to appear free of readily detectable impurities as determined by standard methods of analysis, such as thin layer chromatography (TLC), gel electrophoresis, high performance liquid chromatography (HPLC) and mass spectrometry (MS), used by those of skill in the art to assess such purity, or sufficiently pure such that further purification would not detectably alter the physical and chemical properties, such as enzymatic and biological activities, of the substance. Methods for purification of the compounds to produce substantially chemically pure compounds are known to those of skill in the art. A substantially chemically pure compound may, however, be a mixture of stereoisomers. In such instances, further purification might increase the specific activity of the compound.

As used herein, the nomenclature alkyl, alkoxy, carbonyl, *etc.* is used as is generally understood by those of skill in this art.

As used herein, alkyl, alkenyl and alkynyl carbon chains, if not specified, contain from 1 to 20 carbons, or 1 to 16 carbons, and are straight or branched. Alkenyl carbon chains of from 2 to 20 carbons, in certain embodiments, contain 1 to 8 double bonds, and the alkenyl carbon chains of 2 to 16 carbons, in certain embodiments, contain 1 to 5 double bonds. Alkynyl carbon chains of from 2 to 20 carbons, in certain embodiments, contain 1 to 8 triple bonds, and the alkynyl carbon chains

of 2 to 16 carbons, in certain embodiments, contain 1 to 5 triple bonds. Exemplary alkyl, alkenyl and alkynyl groups herein include, but are not limited to, methyl, ethyl, propyl, isopropyl, isobutyl, n-butyl, sec-butyl, tert-butyl, isopentyl, neopentyl, tert-penytyl and isohexyl. As used herein, lower alkyl, lower alkenyl, and lower alkynyl refer to carbon chains having from about 1 or about 2 carbons up to about 6 carbons. As used herein, "alk(en)(yn)yl" refers to an alkyl group containing at least one double bond and at least one triple bond.

As used herein, "cycloalkyl" refers to a saturated mono- or multicyclic ring system, in certain embodiments of 3 to 10 carbon atoms, in other embodiments of 3 to 6 carbon atoms; cycloalkenyl and cycloalkynyl refer to mono- or multicyclic ring systems that respectively include at least one double bond and at least one triple bond. Cycloalkenyl and cycloalkynyl groups may, in certain embodiments, contain 3 to 10 carbon atoms, with cycloalkenyl groups, in further embodiments, containing 4 to 7 carbon atoms and cycloalkynyl groups, in further embodiments, containing 8 to 10 carbon atoms. The ring systems of the cycloalkyl, cycloalkenyl and cycloalkynyl groups may be composed of one ring or two or more rings which may be joined together in a fused, bridged or spiro-connected fashion. "Cycloalk(en)(yn)yl" refers to a cycloalkyl group containing at least one double bond and at least one triple bond.

As used herein, "substituted alkyl," "substituted alkenyl," "substituted alkynyl," "substituted cycloalkyl," "substituted cycloalkenyl," and "substituted cycloalkynyl" refer to alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl and cycloalkynyl groups, respectively, that are substituted with one or more substituents, in certain embodiments one to three or four substituents, where the substituents are as defined herein, generally selected from Q^1.

As used herein, "aryl" refers to aromatic monocyclic or multicyclic groups containing from 6 to 19 carbon atoms. Aryl groups include, but

are not limited to groups such as fluorenyl, substituted fluorenyl, phenyl, substituted phenyl, naphthyl and substituted naphthyl.

As used herein, "heteroaryl" refers to a monocyclic or multicyclic aromatic ring system, in certain embodiments, of about 5 to about 15 members where one or more, in one embodiment 1 to 3, of the atoms in the ring system is a heteroatom, that is, an element other than carbon, including but not limited to, nitrogen, oxygen or sulfur. The heteroaryl group may be optionally fused to a benzene ring. Heteroaryl groups include, but are not limited to, furyl, imidazolyl, pyrrolidinyl, pyrimidinyl, tetrazolyl, thienyl, pyridyl, pyrrolyl, N-methylpyrrolyl, quinolinyl and isoquinolinyl.

As used herein, a "heteroarylium" group is a heteroaryl group that is positively charged on one or more of the heteroatoms.

As used herein, "heterocyclyl" refers to a monocyclic or multicyclic non-aromatic ring system, in one embodiment of 3 to 10 members, in another embodiment of 4 to 7 members, in a further embodiment of 5 to 6 members, where one or more, in certain embodiments, 1 to 3, of the atoms in the ring system is a heteroatom, that is, an element other than carbon, including but not limited to, nitrogen, oxygen or sulfur. In embodiments where the heteroatom(s) is(are) nitrogen, the nitrogen is optionally substituted with alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, heteroaralkyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, acyl, guanidino, or the nitrogen may be quaternized to form an ammonium group where the substituents are selected as above.

As used herein, "substituted aryl," "substituted heteroaryl" and "substituted heterocyclyl" refer to aryl, heteroaryl and heterocyclyl groups, respectively, that are substituted with one or more substituents, in certain embodiments one to three or four substituents, where the substituents are as defined herein, generally selected from Q^1.

As used herein, "aralkyl" refers to an alkyl group in which one of the hydrogen atoms of the alkyl is replaced by an aryl group.

As used herein, "heteroaralkyl" refers to an alkyl group in which one of the hydrogen atoms of the alkyl is replaced by a heteroaryl group.

As used herein, "halo", "halogen" or "halide" refers to F, Cl, Br or I.

As used herein, pseudohalides or pseudohalo groups are groups that behave substantially similar to halides. Such compounds can be used in the same manner and treated in the same manner as halides. Pseudohalides include, but are not limited to, cyanide, cyanate, thiocyanate, selenocyanate, trifluoromethoxy, and azide.

As used herein, "haloalkyl" refers to an alkyl group in which one or more of the hydrogen atoms are replaced by halogen. Such groups include, but are not limited to, chloromethyl, trifluoromethyl and 1-chloro-2-fluoroethyl.

As used herein, "haloalkoxy" refers to RO- in which R is a haloalkyl group.

As used herein, "sulfinyl" or "thionyl" refers to -S(O)-. As used herein, "sulfonyl" or "sulfuryl" refers to $-S(O)_2-$. As used herein, "sulfo" refers to $-S(O)_2O-$.

As used herein, "carboxy" refers to a divalent radical, -C(O)O-.

As used herein, "aminocarbonyl" refers to $-C(O)NH_2$.

As used herein, "alkylaminocarbonyl" refers to -C(O)NHR in which R is alkyl, including lower alkyl. As used herein, "dialkylaminocarbonyl" refers to -C(O)NR'R in which R' and R are independently alkyl, including lower alkyl; "carboxamide" refers to groups of formula -NR'COR in which R' and R are independently alkyl, including lower alkyl.

As used herein, "diarylaminocarbonyl" refers to -C(O)NRR' in which R and R' are independently selected from aryl, including lower aryl, such as phenyl.

As used herein, "arylalkylaminocarbonyl" refers to -C(O)NRR' in which one of R and R' is aryl, including lower aryl, such as phenyl, and the other of R and R' is alkyl, including lower alkyl.

As used herein, "arylaminocarbonyl" refers to -C(O)NHR in which R is aryl, including lower aryl, such as phenyl.

As used herein, "hydroxycarbonyl" refers to -COOH.

As used herein, "alkoxycarbonyl" refers to -C(O)OR in which R is alkyl, including lower alkyl.

As used herein, "aryloxycarbonyl" refers to -C(O)OR in which R is aryl, including lower aryl, such as phenyl.

As used herein, "alkoxy" and "alkylthio" refer to RO- and RS-, in which R is alkyl, including lower alkyl.

As used herein, "aryloxy" and "arylthio" refer to RO- and RS-, in which R is aryl, including lower aryl, such as phenyl.

As used herein, "alkylene" refers to a straight, branched or cyclic, in certain embodiments straight or branched, divalent aliphatic hydrocarbon group, in one embodiment having from 1 to about 20 carbon atoms, in another embodiment having from 1 to 12 carbons. In a further embodiment alkylene includes lower alkylene. There may be optionally inserted along the alkylene group one or more oxygen, sulfur, including S(=O) and $S(=O)_2$ groups, or substituted or unsubstituted nitrogen atoms, including -NR- and $-N^+RR-$ groups, where the nitrogen substituent(s) is(are) alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl or COR', where R' is alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, -OY or -NYY, where Y is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl or heterocyclyl. Alkylene groups include, but are not limited to, methylene ($-CH_2-$), ethylene ($-CH_2CH_2-$), propylene ($-(CH_2)_3-$), methylenedioxy ($-O-CH_2-O-$) and ethylenedioxy ($-O-(CH_2)_2-O-$). The term "lower alkylene" refers to alkylene groups having 1 to 6 carbons. In certain embodiments, alkylene groups are lower alkylene, including alkylene of 1 to 3 carbon atoms.

As used herein, "azaalkylene" refers to $-(CRR)_n-NR-(CRR)_m-$, where n and m are each independently an integer from 0 to 4. As used herein, "oxaalkylene" refers to $-(CRR)_n-O-(CRR)_m-$, where n and m are each independently an integer from 0 to 4. As used herein, "thiaalkylene"

refers to $-(CRR)_n-S-(CRR)_m-$, $-(CRR)_n-S(=O)-(CRR)_m-$, and $-(CRR)_n-S(=O)_2-(CRR)_m-$, where n and m are each independently an integer from 0 to 4.

As used herein, "alkenylene" refers to a straight, branched or cyclic, in one embodiment straight or branched, divalent aliphatic hydrocarbon group, in certain embodiments having from 2 to about 20 carbon atoms and at least one double bond, in other embodiments 1 to 12 carbons. In further embodiments, alkenylene groups include lower alkenylene. There may be optionally inserted along the alkenylene group one or more oxygen, sulfur or substituted or unsubstituted nitrogen atoms, where the nitrogen substituent is alkyl. Alkenylene groups include, but are not limited to, $-CH=CH-CH=CH-$ and $-CH=CH-CH_2-$. The term "lower alkenylene" refers to alkenylene groups having 2 to 6 carbons. In certain embodiments, alkenylene groups are lower alkenylene, including alkenylene of 3 to 4 carbon atoms.

As used herein, "alkynylene" refers to a straight, branched or cyclic, in certain embodiments straight or branched, divalent aliphatic hydrocarbon group, in one embodiment having from 2 to about 20 carbon atoms and at least one triple bond, in another embodiment 1 to 12 carbons. In a further embodiment, alkynylene includes lower alkynylene. There may be optionally inserted along the alkynylene group one or more oxygen, sulfur or substituted or unsubstituted nitrogen atoms, where the nitrogen substituent is alkyl. Alkynylene groups include, but are not limited to, $-C\equiv C-C\equiv C-$, $-C\equiv C-$ and $-C\equiv C-CH_2-$. The term "lower alkynylene" refers to alkynylene groups having 2 to 6 carbons. In certain embodiments, alkynylene groups are lower alkynylene, including alkynylene of 3 to 4 carbon atoms.

As used herein, "alk(en)(yn)ylene" refers to a straight, branched or cyclic, in certain embodiments straight or branched, divalent aliphatic hydrocarbon group, in one embodiment having from 2 to about 20 carbon atoms and at least one triple bond, and at least one double bond; in

another embodiment 1 to 12 carbons. In further embodiments, alk(en)(yn)ylene includes lower alk(en)(yn)ylene. There may be optionally inserted along the alkynylene group one or more oxygen, sulfur or substituted or unsubstituted nitrogen atoms, where the nitrogen substituent is alkyl. Alk(en)(yn)ylene groups include, but are not limited to, $-C=C-(CH_2)_n-C\equiv C-$, where n is 1 or 2. The term "lower alk(en)(yn)ylene" refers to alk(en)(yn)ylene groups having up to 6 carbons. In certain embodiments, alk(en)(yn)ylene groups have about 4 carbon atoms.

As used herein, "cycloalkylene" refers to a divalent saturated mono- or multicyclic ring system, in certain embodiments of 3 to 10 carbon atoms, in other embodiments 3 to 6 carbon atoms; cycloalkenylene and cycloalkynylene refer to divalent mono- or multicyclic ring systems that respectively include at least one double bond and at least one triple bond. Cycloalkenylene and cycloalkynylene groups may, in certain embodiments, contain 3 to 10 carbon atoms, with cycloalkenylene groups in certain embodiments containing 4 to 7 carbon atoms and cycloalkynylene groups in certain embodiments containing 8 to 10 carbon atoms. The ring systems of the cycloalkylene, cycloalkenylene and cycloalkynylene groups may be composed of one ring or two or more rings which may be joined together in a fused, bridged or spiro-connected fashion. "Cycloalk(en)(yn)ylene" refers to a cycloalkylene group containing at least one double bond and at least one triple bond.

As used herein, "substituted alkylene," "substituted alkenylene," "substituted alkynylene," "substituted cycloalkylene," "substituted cycloalkenylene," and "substitued cycloalkynylene" refer to alkylene, alkenylene, alkynylene, cycloalkylene, cycloalkenylene and cycloalkynylene groups, respectively, that are substituted with one or more substituents, in certain embodiments one to three or four substituents, where the substituents are as defined herein, generally selected from Q^1.

As used herein, "arylene" refers to a monocyclic or polycyclic, in certain embodiments monocyclic, divalent aromatic group, in one embodiment having from 5 to about 20 carbon atoms and at least one aromatic ring, in another embodiment 5 to 12 carbons. In further embodiments, arylene includes lower arylene. Arylene groups include, but are not limited to, 1,2-, 1,3- and 1,4-phenylene. The term "lower arylene" refers to arylene groups having 5 or 6 carbons.

As used herein, "heteroarylene" refers to a divalent monocyclic or multicyclic aromatic ring system, in one embodiment of about 5 to about 15 members where one or more, in certain embodiments 1 to 3, of the atoms in the ring system is a heteroatom, that is, an element other than carbon, including but not limited to, nitrogen, oxygen or sulfur.

As used herein, "heterocyclylene" refers to a divalent monocyclic or multicyclic non-aromatic ring system, in certain embodiments of 3 to 10 members, in one embodiment 4 to 7 members, in another embodiment 5 to 6 members, where one or more, including 1 to 3, of the atoms in the ring system is a heteroatom, that is, an element other than carbon, including but not limited to, nitrogen, oxygen or sulfur.

As used herein, "substituted arylene," "substituted heteroarylene" and "substituted heterocyclylene" refer to arylene, heteroarylene and heterocyclylene groups, respectively, that are substituted with one or more substituents, in certain embodiments one to three of four substituents, where the substituents are as defined herein, generally selected from Q^1.

As used herein, "alkylidene" refers to a divalent group, such as $=CR'R''$, which is attached to one atom of another group, forming a double bond. Alkylidene groups include, but are not limited to, methylidene ($=CH_2$) and ethylidene ($=CHCH_3$). As used herein, "arylalkylidene" refers to an alkylidene group in which either R' or R" is an aryl group. "Cycloalkylidene" groups are those where R' and R" are linked to form a carbocyclic ring. "Heterocyclylidene" groups are those

where at least one of R' and R" contain a heteroatom in the chain, and R' and R" are linked to form a heterocyclic ring.

As used herein, "amido" refers to the divalent group -C(O)NH-. "Thioamido" refers to the divalent group -C(S)NH-. "Oxyamido" refers to the divalent group -OC(O)NH-. "Thiaamido" refers to the divalent group -SC(O)NH-. "Dithiaamido" refers to the divalent group -SC(S)NH-. "Ureido" refers to the divalent group -HNC(O)NH-. "Thioureido" refers to the divalent group -HNC(S)NH-.

As used herein, "semicarbazide" refers to -NHC(O)NHNH-. "Carbazate" refers to the divalent group -OC(O)NHNH-. "Isothiocarbazate" refers to the divalent group -SC(O)NHNH-. "Thiocarbazate" refers to the divalent group -OC(S)NHNH-. "Sulfonylhydrazide" refers to the group -SO_2NHNH-. "Hydrazide" refers to the divalent group -C(O)NHNH-. "Azo" refers to the divalent group -N=N-. "Hydrazinyl" refers to the divalent group -NH-NH-.

Where the number of any given substituent is not specified (*e.g.*, "haloalkyl"), there may be one or more substituents present. For example, "haloalkyl" may include one or more of the same or different halogens. As another example, "C_{1-3}alkoxyphenyl" may include one or more of the same or different alkoxy groups containing one, two or three carbons.

As used herein, the following terms have their accepted meaning in the chemical literature:

AcOH	acetic acid
Cbz	benzyl carbamate
CDI	carbonyl diimidazole
$CHCl_3$	chloroform
conc	concentrated
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
DME	1,2-dimethoxyethane

DMF	*N,N*-dimethylformamide
DMSO	dimethylsulfoxide
EtOAc	ethyl acetate
EtOH	ethanol (100%)
Et_2O	diethyl ether
Hex	hexanes
H_2SO_4	sulfuric acid
MeCN	acetonitrile
MeOH	methanol
Pd (0)	palladium (0)
Pd/C	palladium on activated carbon
PPh_3	triphenyl phosphine
TEA	triethylamine
THF	tetrahydrofuran
TFA	trifluoroacetic acid

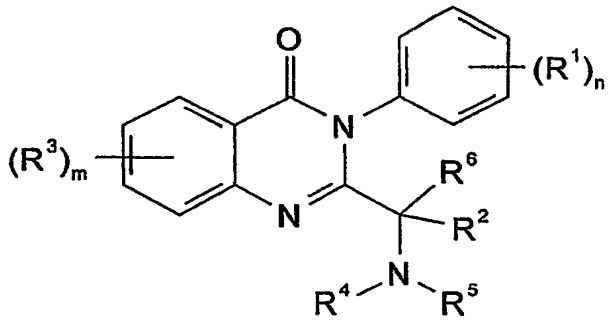
As used herein, the abbreviations for any protective groups, amino acids and other compounds, are, unless indicated otherwise, in accord with their common usage, recognized abbreviations, or the IUPAC-IUB Commission on Biochemical Nomenclature (see, (1972) *Biochem.* *11*:942-944).

B. Quinazolinone Modulators of Nuclear Receptors

Compounds for use in compositions and methods for modulating the activity of nuclear receptors are provided. In particular, compounds for use in compositions and methods for modulating farnesoid X receptor (FXR) and/or orphan nuclear receptors, are provided.

In one embodiment, the compounds have formula I, where R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, or substituted or unsubstituted aralkyl. In another embodiment, R^7 is hydrogen, substituted or unsubstituted alkyl, aryl, or aralkyl. In another embodiment, R^7 is hydrogen, methyl, ethyl, propyl, 2-methoxyethyl, benzyl, or naphthyl.

In one embodiment, the compounds for use in the compositions and methods provided herein have formula I where R^7 is substituted or unsubstituted phenyl. In another embodiment, the compounds have formula II:



wherein:

each R^1 and R^3 are independently selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2, with the proviso that R^1 is not 4-$C(OH)(CF_3)_2$; or any two R^1 groups or R^3 groups, which substitute adjacent carbons on the ring, together with atoms to which they are attached, form substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted heteroaryl, or substituted or unsubstituted aryl;

n is an integer from 0 to 5;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, C(D)R^{15} where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl, or R^{18} and R^{19} together for alkylene, alkenylene or alkyleneoxyalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl,

substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or $C(D)R^{15}$ where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen or substituted or unsubstituted alkyl; or (ii) R^2 and R^6 together form alkylene or alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted

alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or

unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or

unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^1-R^6, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,

hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy (*i.e.*, -O-$(CH_2)_y$-O-), thioalkylenoxy (*i.e.*, -S-$(CH_2)_y$-O-) or alkylenedithioxy (*i.e.*, -S-$(CH_2)_y$-S-) where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -$NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -$NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl,

aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^{+}R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or

alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy (*i.e.*, -O-$(CH_2)_y$-O-), thioalkylenoxy (*i.e.*, -S-$(CH_2)_y$-O-) or alkylenedithioxy (*i.e.*, -S-$(CH_2)_y$-S-) where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene.

In another embodiment, any two R^1 groups or R^3 groups, which substitute adjacent carbons on the ring, together with atoms to which they are attached, form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkylenedioxy, substituted or unsubstituted thioalkylenoxy, or substituted or unsubstituted alkylenedithioxy.

In one embodiment, R^1 is not -C(OH)$(CF_3)_2$. In another embodiment, R^6 is hydrogen. In another embodiment, n is 0, 1 or 2. In another embodiment, m is 1.

In another embodiment, the compounds are of formula II, where each R^1 is independently halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted dialkylamino, substituted or unsubstituted aralkoxy, hydroxy, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclyl or substituted or unsubstituted cycloalkyl.

In another embodiment, each R^1 is independently halo; pseudohalo; alkyl; haloalkyl; alkoxy; haloalkoxy; heterocyclylalkoxy; alkoxyalkoxy; aryl; aryl substituted with alkyl, halo, -COOH, alkoxy, pseudohalo or -COO-alkyl; dialkylamino; aralkoxy; hydroxy; heteroaryl; heterocyclyl; or cycloalkyl.

In another embodiment, each R^1 is independently chloro, fluoro, ethyl, methyl, methoxy, bromo, cyano, phenyl, tert-butyl, trifluoromethoxy, dimethylamino, trifluoromethyl, benzyloxy, hydroxy, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-

methoxyphenyl, ethoxy, isopropoxy, butoxy, isobutoxy, 2-(N-morpholino)ethoxy, 2-methoxyethoxy, 4-cyanophenyl, 2-thienyl, 3-thienyl, 3-methoxycarbonylphenyl, 4-methoxycarbonylphenyl, 3-hydroxycarbonylphenyl, N-pyrrolidinyl, or N-morpholinyl.

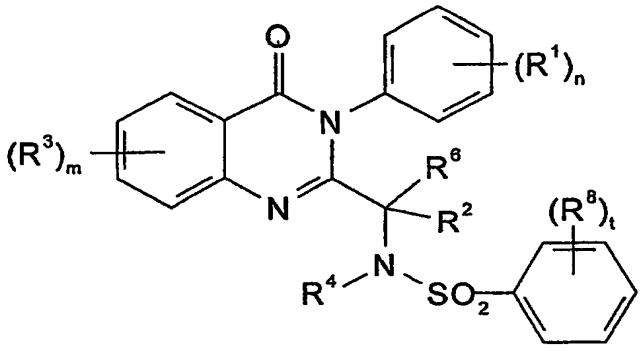
In another embodiment, R^2 is hydrogen or substituted or unsubstituted alkyl, and R^6 is hydrogen. In another embodiment, R^2 is hydrogen or alkyl. In another embodiment, R^2 is hydrogen, methyl or ethyl.

In another embodiment, each R^3 is independently substituted or unsubstituted alkyl, halo, pseudohalo, substituted or unsubstituted alkoxy, hydroxy, substituted or unsubstituted aralkoxy, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclyl, or substituted or unsubstituted cycloalkyl.

In another embodiment, each R^3 is independently alkyl; halo; alkoxy; hydroxy; aralkoxy; aryl; heteroaryl; alkoxycarbonylalkoxy; aryl substituted with alkyl, halo, pseudohalo, alkoxy, -COOH or -COO-alkyl; or heterocyclyl.

In another embodiment, each R^3 is independently methyl, chloro, methoxy, hydroxy, bromo, ethoxy, isopropoxy, isobutoxy, butoxy, benzyloxy, ethoxycarbonylmethoxy, phenyl, 2-thienyl, 3-thienyl, 2-methylphenyl, 3-methylphenyl, 4-methylpheny, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3-methoxyphenyl, 4-methoxyphenyl, 4-hydroxycarbonylphenyl, N-pyrrolidinyl, N-morpholinyl, 3-methoxycarbonylphenyl, 4-methoxycarbonylphenyl, 3-hydroxycarbonylphenyl, 4-cyanophenyl, or piperidinyl.

In another embodiment, one of R^4 and R^5 is $-SO_2-$(substituted or unsubstituted aryl). In another embodiment, one of R^4 and R^5 is $-SO_2-$(substituted or unsubstituted phenyl). In another embodiment, the compounds for use in the compositions and methods provided herein have formula III:



where R^1, R^2, R^3, R^4, R^6, n and m are as defined above; t is an integer from 0 to 5; each R^8 is independently substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted heteroaryl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, halo, pseudohalo; or any two R^8 substituents, which substitute adjacent atoms on the ring, together form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl ring having 5 or 6 members in the ring and where the heteroatoms, if present, are selected from O, S and substituted or unsubstituted N; where R^8, when substituted, is substituted with one or more, in one embodiment one to five, in another embodiment one, two or three, substituents each independently selected from Q^1, as defined above.

In another embodiment, any two R^8 substituents, which substitute adjacent atoms on the ring, together form $-N=CR^{70}-CR^{70}=CR^{70}-$ or $-CR^{70}=CR^{70}-CR^{70}=CR^{70}-$, where each R^{70} is independently hydrogen, halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, or substituted or unsubstituted heteroaralkyl;

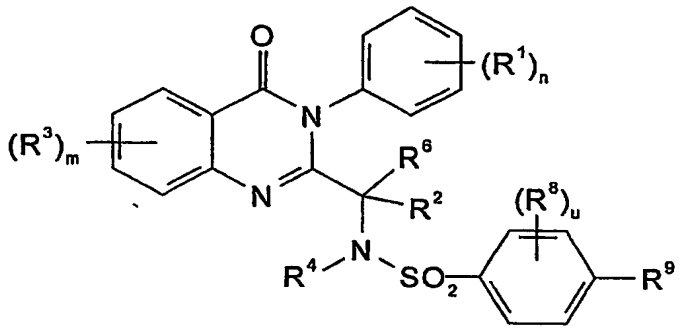
where R^8 and R^{70}, when substituted, are substituted with one or more, in one embodiment one to five, in another embodiment one, two or three, substituents each independently selected from Q^1, as defined above.

In another embodiment, the compounds have formula III, where each R^8 is independently alkyl, alkoxy, haloalkoxy, heterocyclyl, heteroaryl, halo, haloalkyl, aryl or pseudohalo; or any two R^8 groups, which substitute adjacent carbons on the ring, together form -N=CH-CH=CH- or -CH=CH-CH=CH-.

In another embodiment, each R^8 is independently tert-butyl, methoxy, methyl, trifluoromethoxy, 2-thienyl, fluoro, chloro, trifluoromethyl, phenyl, cyano, n-propyl, 1,1-dimethylpropyl, isopropyl, butoxy or n-butyl; or any two R^8 groups, which substitute adjacent carbons on the ring, together form -N=CH-CH=CH- or -CH=CH-CH=CH-.

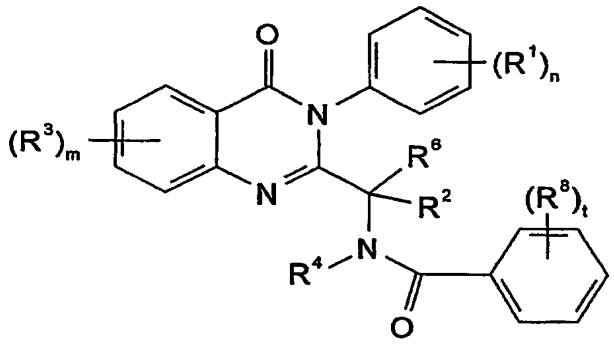
In another embodiment, the compounds have formula III where R^4 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, or substituted or unsubstituted heteroaralkyl. In another embodiment, R^4 is hydrogen, alkyl, aralkyl or heteroaralkyl. In another embodiment, R^4 is hydrogen, methyl, 2-methoxy-1-ethyl, propyl, isobutyl, butyl, pentyl, isopentyl, hexyl, benzyl, phenethyl or 2-thienylmethyl.

In another embodiment, one R^8 group is 4-tert-butyl or 4-isopropyl. In another embodiment, the compounds for use in the compositions and methods provided herein have formula IV:



where R^1, R^2, R^3, R^4, R^6, R^8, m and n are selected as above; u is an integer from 0 to 4; and R^9 is tert-butyl or isopropyl. In another embodiment, R^9 is tert-butyl. In another embodiment, R^9 is isopropyl.

In another embodiment, one of R^4 and R^5 is -C(O)-(substituted or unsubstituted aryl). In another embodiment, one of R^4 and R^5 is -C(O)-(substituted or unsubstituted phenyl). In another embodiment, the compounds for use in the compositions and methods provided herein have formula V:



where R^1, R^2, R^3, R^4, R^6, R^8, t, n and m are as defined above.

In another embodiment, the compounds have formula V where each R^1 is independently halo, substituted or unsubstituted alkyl, or substituted or unsubstituted alkoxy, where the substituents, when present, are selected from Q^1, as defined above. In another embodiment, each R^1 is independently alkoxy, alkyl or halo. In another embodiment, each R^1 is independently methoxy, methyl, chloro or fluoro.

In another embodiment, the compounds have formula V where R^2 is hydrogen or substituted or unsubstituted alkyl, where the substituents, when present, are selected from Q^1, as defined above. In another embodiment, R^2 is hydrogen or alkyl. In another embodiment, R^2 is hydrogen or methyl.

In another embodiment, the compounds have formula V where each R^3 is independently hydrogen or substituted or unsubstituted alkoxy, where the substituents, when present, are selected from Q^1, as defined above. In another embodiment, each R^3 is independently hydrogen or alkoxy. In another embodiment, each R^3 is independently hydrogen or methoxy.

In another embodiment, the compounds have formula V where R^4 is substituted or unsubstituted alkyl, where the substituents, when present, are selected from Q^1, as defined above. In another embodiment, R^4 is alkyl. In another embodiment, R^4 is butyl or methyl.

In another embodiment, the compounds have formula V where R^6 is hydrogen.

In another embodiment, the compounds have formula V where each R^8 is independently substituted or unsubstituted alkyl, where the substituents, when present, are selected from Q^1, as defined above. In another embodiment, each R^8 is alkyl. In another embodiment, R^8 is tert-butyl.

In another embodiment, one of R^4 and R^5 is -C(O)-(substituted or unsubstituted alkyl), where the substituents, when present, are selected from Q^1, as defined above, and the other of R^4 and R^5 is selected from hydrogen and substituted or unsubstituted alkyl, where the substituents, when present, are selected from Q^1, as defined above. In another embodiment, one of R^4 and R^5 is -C(O)-alkyl, and the other is alkyl. In another embodiment, one of R^4 and R^5 is -C(O)-octyl, and the other is methyl or butyl.

In another embodiment, one of R^4 and R^5 is $-C(O)-NR^{80}R^{81}$, where R^{80} and R^{81} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; or R^{80} and R^{81} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; where R^{80} and R^{81} are each independently unsubstituted or substituted with one or more, in one embodiment one to five, in another embodiment one, two or three, substituents each independently selected from Q^1, as defined above, and the other of R^4 and R^5 is selected from hydrogen and substituted or unsubstituted alkyl, where the substituents, when present, are selected from Q^1, as defined above. In another embodiment, the other of R^4 and R^5 is alkyl. In another embodiment, the other of R^4 and R^5 is methyl or butyl.

In another embodiment, R^{80} and R^{81} are each independently selected from hydrogen, substituted or unsubstituted cycloalkyl, and substituted or unsubstituted aryl. In another embodiment, R^{80} is hydrogen. In another embodiment, R^{81} is cyclohexyl, 4-nitrophenyl, 2-methoxyphenyl, 3-cyanophenyl, 3,4-dichlorophenyl, 2,6-diisopropylphenyl, 2-methylphenyl, 2-trifluoromethylphenyl, 2-fluorophenyl, 3-fluorophenyl, 3-methylphenyl, 3-chlorophenyl, 2,6-dimethylphenyl or 3-trifluoromethylphenyl.

In another embodiment, R^4 and R^5 together form substituted or unsubstituted alkyleneazaalkylene, where the substituents, if present, are each independently selected from Q^1, as defined above. In one embodiment, there are one, two or three Q^1 substituents. In another embodiment, R^4 and R^5 together form $-CH_2-CHMe-N(R^{90})-CH_2-CH_2-$, where

R^{90} is substituted or unsubstituted heteroarylcarbonyl, substituted or unsubstituted alkylcarbonyl, substituted or unsubstituted arylcarbonyl, substituted or unsubstituted arylsulfonyl, substituted or unsubstituted alkylaminocarbonyl, or substituted or unsubstituted arylaminocarbonyl.

In another embodiment, R^{90} is 2-thienylcarbonyl, butyryl, 4-fluorobenzoyl, benzyloxyacetyl, diphenylacetyl, 4-nitrobenzoyl, 2,5-dichlorobenzenesulfonyl, tert-butylaminocarbonyl, 4-tert-butylphenylsulfonyl, phenylaminocarbonyl, 2,3-dichlorophenylaminocarbonyl or 3,4-methylenedioxybenzoyl.

In another embodiment, the compounds for use in the compositions and methods provided herein have any of formulae I-V, where Q^2 is halo, pseudohalo, aralkoxy or nitro; or any two Q^2 groups, which substitute adjacent carbons, together form alkylenedioxy. In another embodiment, Q^2 is nitro, fluoro, benzyloxy or chloro; or two Q^2 groups, which substitute adjacent carbons, together form methylenedioxy.

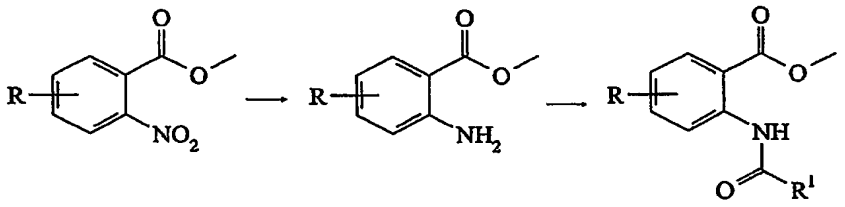
C. Preparation of the compounds

Starting materials in the synthesis examples provided herein are either available from commercial sources or *via* literature procedures. All commercially available compounds were used without further purification unless otherwise indicated. $CDCl_3$ (99.8% D, Cambridge Isotope Laboratories) was used in all experiments as indicated. Proton (^1H) nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance 400 MHz NMR spectrometer. Significant peaks are tabulated and typically include: number of protons, and multiplicity (s, singlet; d, double; t, triplet; q, quartet; m, multiplet; br s, broad singlet). Chemical shifts are reported as parts per million (δ) relative to tetramethylsilane. Low resolution mass spectra (MS) were obtained as electrospray ionization (ESI) mass spectra, which were recorded on a Perkin-Elmer SCIEX HPLC/MS instrument using reverse-phase conditions (acetonitrile/water, 0.05% trifluoroacetic acid). Flash chromatography

was performed using Merck Silica Gel 60 (230-400 mesh) following standard protocol (Still *et al.* (1978) *J. Org. Chem. 43*, 2923).

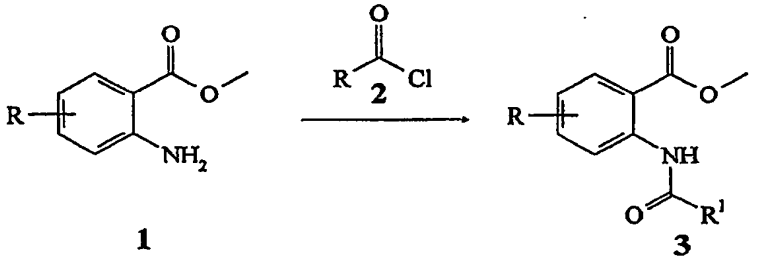
Substituted methyl-anthranilates are commercially available or can be synthetically obtained from commercially available starting materials, using standard literature protocols (Scheme 1) in which R is typically a halogen, alkyl, or alkoxy.

Scheme 1



N-acyl methyl anthranilates **3** are prepared by treating methyl anthranilate **1** with an acid chloride **2** in which R^1 is typically alkyl, aryl, or heteroaryl (Scheme 2). Acid chlorides are commercially available and/or can be prepared using standard methods found in literature. R^1 is typically 1-chloroethyl or a product derived from protected amino acids

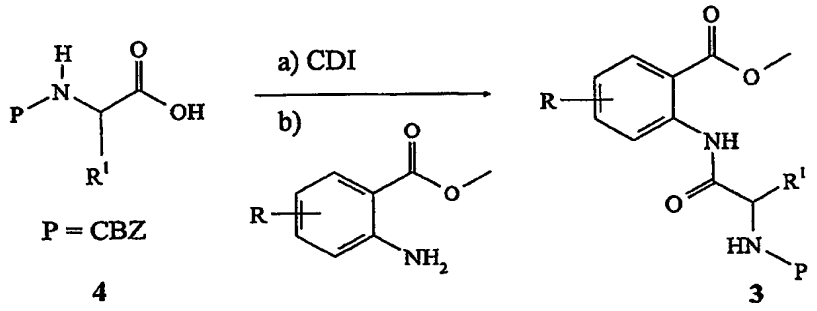
Scheme 2



e.g., N-CBZ glycine. In the case where protected amino acids are used alternative acylation conditions were required (Yu, Melvin, *et al.* (1992) *J. Med. Chem. 35*:2534-2542). For example, the protected amino acid 4 is treated with carbonyl diimidazole (CDI) followed by subsequent treatment of a substituted methyl anthranilate 1 to yield the N-acyl methyl

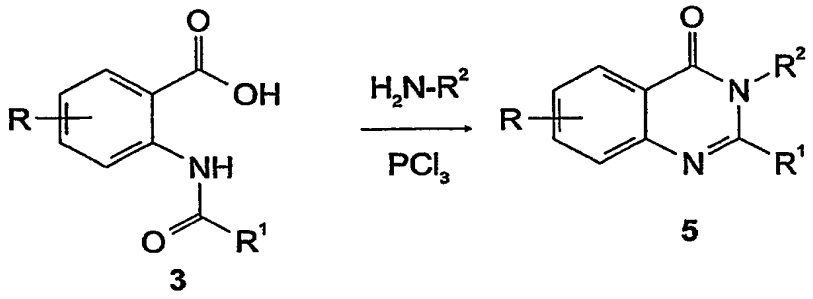
anthranilate **3** (Scheme 3). Once again, chemical diversity is realized by varying R and R^1 as previously described.

Scheme 3



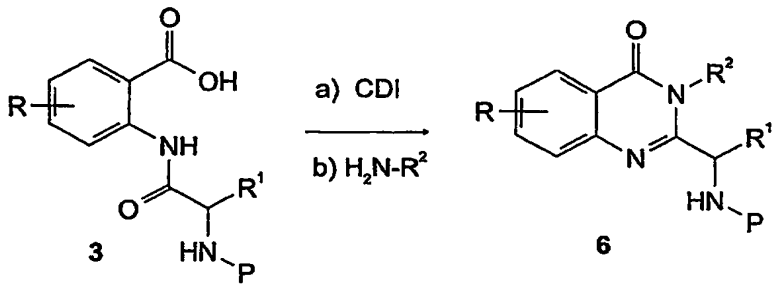
The quinazolinone core **5** was prepared by acylating an amine with the N-acyl anthranilic acid followed by a tandem cyclodehydration via thermolysis (Rao *et al.* (1985) *J. Indian Chem.*:234-237. N-Acyl anthranilic acid **3** was treated with phosphorous trichloride and an amine, under refluxing conditions, to afford the desired quinazolinones **5** (Scheme 4) in which R^2 typically includes an aryl (aniline), heteroaryl, or primary amines. When **3** possesses a protected amino appendage alternative conditions were required to generate the core (**6**)(Yu *et al.* (1992) *J. Med. Chem. 35*:2534-2542).

Scheme 4

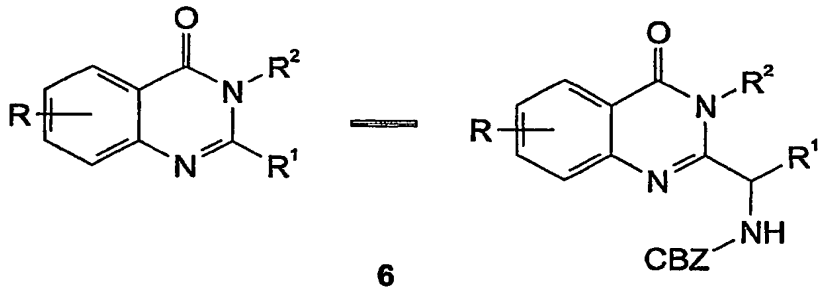


For example, compound **3** was treated with carbonyl diimidazole in which the resulting activated acid was treated with an amine (R^2NH_2) under refluxing conditions to yield the quinazolinone **6** (Scheme 5).

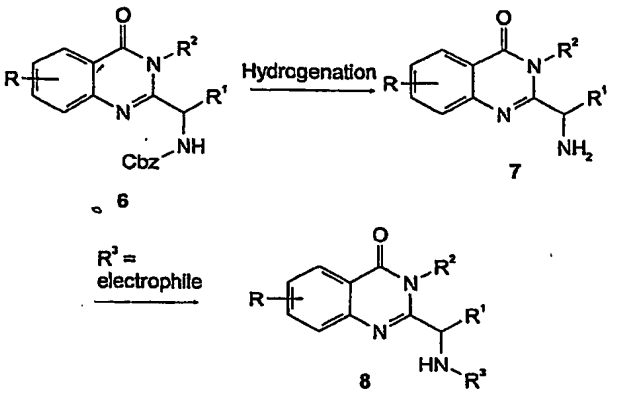
Scheme 5



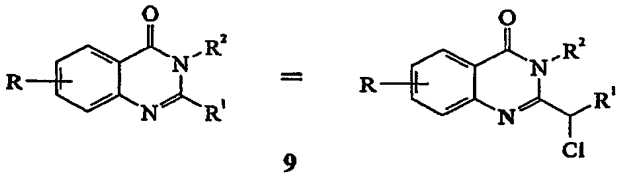
The protected amino appendage was then deprotected using standard conditions found in literature reference (Greene *et al. Protective Groups in Organic Synthesis,* 3rd Ed. (John Wiley, NY (1999))). For example, compound **5** was subjected to hydrogenation conditions to yield a free amine **7** (Scheme 6). Subsequently, the free amine was treated with a number of differing electrophiles (R^3) to yield a diverse set of quinazolinone analogs (**8**) in which R^3 is typically an amide or sulfonamide but not limited to these groups. Additional electrophiles include carboxylic acids and derivatives thereof, sulfonyl chlorides, isocyanates, alkyl halides, aldehydes, ketones, and chloroformates.



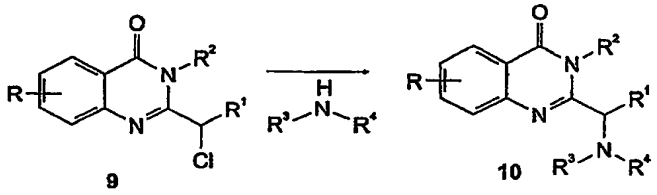
Scheme 6



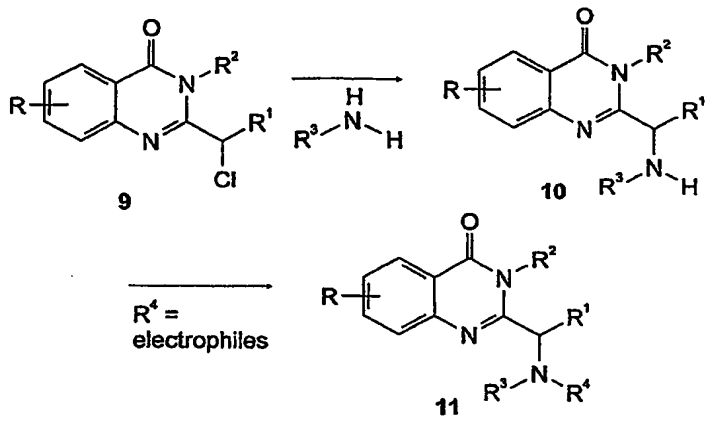
Alternatively, when R^1 is a substituted 1-chloroalkyl (**9**) various nucleophiles were introduced i.e. amines, alcohols, cuprates etc. For example when 1'-chloro ethyl quinazolinone **9** was treated with an amine under the appropriate conditions, quinazolinone **10** was realized (Scheme 7a). Subsequently, when R^4 is equal to hydrogen, **10** was treated with various electrophiles to yield compounds like **11**, in which R^4 is typically an amide or sulfonamide, but not limited to (Scheme 7b). Additional electrophiles include carboxylic acids and derivatives thereof, sulfonyl chlorides, isocyanates, alkyl halides, aldehydes, ketones, and chloroformates.



Scheme 7a

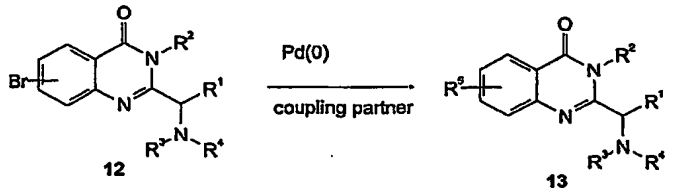


Scheme 7b



An aryl bromide containing quinazolinone (12) can be further manipulated with the addition of diverse structural modifications using standard C-C, C-N, and C-O bond forming reactions. The purpose of this was to gain entry into a diverse set of analogs that were not accessible through previously described methods. For example, a bromo-substituted heterocycle can be manipulated using standard transitions metal chemistries to introduce a large array of diverse functionalities that are otherwise difficult to obtain using alternative methods (Hegedus, Louis, S. *Transition Metals in the Synthesis of Complex Organic Molecules*, University Science Books: Mill Valley, CA (1994)). Quinazolinone 12 was treated with Pd (0) and a phosphorous ligand in the presence of the appropriate coupling partner (R^5) to yield a new series of quniazolinone analogs similar to 13 (Scheme 8). A typical (R^5) monomer would include boronic acids, amines, amides, mono-substituted alkynes, alcohols, or organotin reagents. These monomers are typically aryl, heteroaromatic, and alkyl in nature. In addition, these monomeric reagents are commercially available and/or can be synthesized using known literature methodologies.

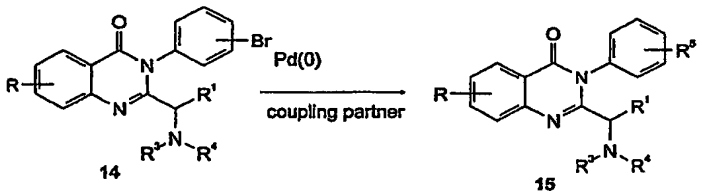
Scheme 8



12 13

Similarly, compound **14** was modified using the same chemistries described above. The conditions and reagents used to modify the N-aryl quinazolinones **14** are identical to those previously described. Compound **14** was treated with Pd (0) and a phosphorous ligand in the presence of an appropriate monomer (R^5) to yield N-aryl substituted quinazolinones like compound **15** (Scheme 9). A typical (R^5) monomer would include boronic acids, amines, amides, mono-substituted alkynes, alcohols, or organotin reagents. These monomers are typically aryl, heteroaromatic, and alkyl in nature. In addition, these monomeric reagents are commercially available and/or can be synthesized using known literature methodologies.

Scheme 9

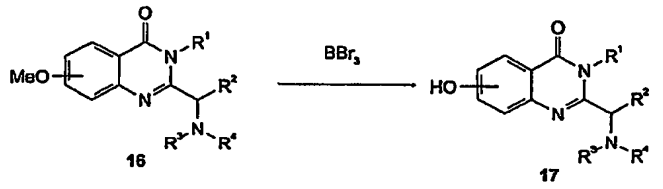


14 15

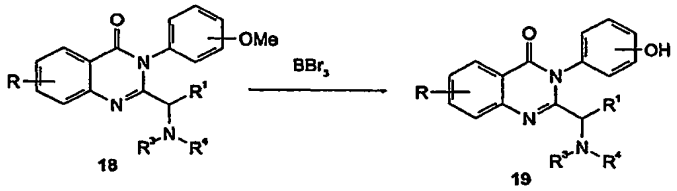
Additional modifications were made to the quinazolinone core by demethylating the methoxy-phenyl ether of quinazolinone **16** to reveal a phenol **17** as handle for a point of diversity. Methoxy phenyl ethers are typically demethylated using a variety of literature methods (McOmie, J. F. W., West, D.E. *Org. Synth.*, Collect. Vol. V, 412 (1973): Jung, M. E., Lyster, M. A., *J. Org. Chem.*, **42**, 3761 (1977)). For example, when **16** is treated with boron tribromide the exclusive formation of phenol **17** was observed (Scheme 10). Similarly, the methoxy substituted N-aryl

quinazolinone **18** was manipulated using the same protocol outlined above to yield compound **19** (Scheme 11).

Scheme 10

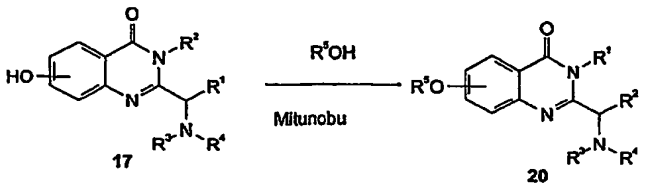


Scheme 11



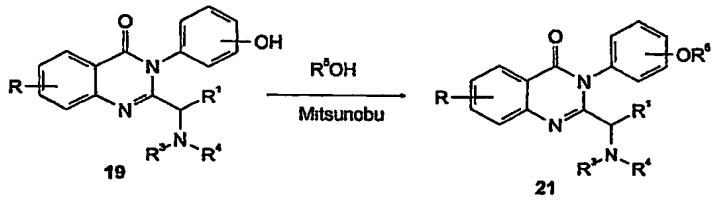
Treatment of a phenol with a variety of electrophiles establishes yet another avenue for diversity to be introduced that was not easily accessible with other methodologies. For example the phenol **17** was treated with various electrophiles, i.e. alkyl halides, isocyanates and acid chlorides to yield ethers, carbamates and esters respectively. Additionally, the phenol **17** was converted to various ethers **20** by utilizing the Mitsunobu reaction (Mitsunobu, O.; Yamada, M. Bull. Chem. Soc. Jpn.,1967, 40,2380; Canp, D.; Jenkins, I.D. Aust. J. Chem., 1988, 41, 1835). Compound **17** was treated with triphenyl phosphine, alcohol (R^5OH) and diisopropyl azodicarboxylate (DIAD) to afford quinazolinone **20** (Scheme 12). Typical alcohols that were used include primary and secondary aliphatic alcohols. However, alcohols containing other functionalities were also used e.g. ethyl glycolate.

Scheme 12



Similarly, compound **19** could be converted in an identical manner as described above to achieve analogs similar to **21**. A large array of diverse functionalities can be introduced that were otherwise difficult to obtain using alternative methods (Scheme 13).

Scheme 13



D. Formulation of pharmaceutical compositions

The pharmaceutical compositions provided herein contain therapeutically effective amounts of one or more of the nuclear receptor activity modulators provided herein that are useful in the prevention, treatment, or amelioration of one or more of the symptoms of diseases or disorders associated with nuclear receptor activity, including FXR and/or orphan nuclear receptor activity. Such diseases or disorders include, but are not limited to, hypercholesterolemia, hyperlipoproteinemia, hypertriglyceridemia, lipodystrophy, hyperglycemia, diabetes mellitus, dyslipidemia, atherosclerosis, gallstone disease, acne vulgaris, acneiform skin conditions, diabetes, Parkinson's disease, cancer, Alzheimer's disease, inflammation, immunological disorders, lipid disorders, obesity, conditions characterized by a perturbed epidermal barrier function, hyperlipidemia, cholestasis, peripheral occlusive disease, ischemic stroke,

conditions of disturbed differentiation or excess proliferation of the epidermis or mucous membrane, and cardiovascular disorders.

The compositions contain one or more compounds provided herein. The compounds are preferably formulated into suitable pharmaceutical preparations such as solutions, suspensions, tablets, dispersible tablets, pills, capsules, powders, sustained release formulations or elixirs, for oral administration or in sterile solutions or suspensions for parenteral administration, as well as transdermal patch preparation and dry powder inhalers. Typically the compounds described above are formulated into pharmaceutical compositions using techniques and procedures well known in the art (see, *e.g.*, Ansel *Introduction to Pharmaceutical Dosage Forms, Fourth Edition* **1985**, 126).

In the compositions, effective concentrations of one or more compounds or pharmaceutically acceptable derivatives is (are) mixed with a suitable pharmaceutical carrier or vehicle. The compounds may be derivatized as the corresponding salts, esters, enol ethers or esters, acids, bases, solvates, hydrates or prodrugs prior to formulation, as described above. The concentrations of the compounds in the compositions are effective for delivery of an amount, upon administration, that treats, prevents, or ameliorates one or more of the symptoms of diseases or disorders associated with nuclear receptor activity or in which nuclear receptor activity is implicated. Such diseases or disorders include, but are not limited to, hypercholesterolemia, hyperlipoproteinemia, hypertriglyceridemia, lipodystrophy, hyperglycemia, diabetes mellitus, dyslipidemia, atherosclerosis, gallstone disease, acne vulgaris, acneiform skin conditions, diabetes, Parkinson's disease, cancer, Alzheimer's disease, inflammation, immunological disorders, lipid disorders, obesity, conditions characterized by a perturbed epidermal barrier function, hyperlipidemia, cholestasis, peripheral occlusive disease, ischemic stroke, conditions of disturbed differentiation or excess proliferation of the epidermis or mucous membrane, and cardiovascular disorders.

Typically, the compositions are formulated for single dosage administration. To formulate a composition, the weight fraction of compound is dissolved, suspended, dispersed or otherwise mixed in a selected vehicle at an effective concentration such that the treated condition is relieved or ameliorated. Pharmaceutical carriers or vehicles suitable for administration of the compounds provided herein include any such carriers known to those skilled in the art to be suitable for the particular mode of administration.

In addition, the compounds may be formulated as the sole pharmaceutically active ingredient in the composition or may be combined with other active ingredients. Liposomal suspensions, including tissue-targeted liposomes, such as tumor-targeted liposomes, may also be suitable as pharmaceutically acceptable carriers. These may be prepared according to methods known to those skilled in the art. For example, liposome formulations may be prepared as described in U.S. Patent No. 4,522,811. Briefly, liposomes such as multilamellar vesicles (MLV's) may be formed by drying down egg phosphatidyl choline and brain phosphatidyl serine (7:3 molar ratio) on the inside of a flask. A solution of a compound provided herein in phosphate buffered saline lacking divalent cations (PBS) is added and the flask shaken until the lipid film is dispersed. The resulting vesicles are washed to remove unencapsulated compound, pelleted by centrifugation, and then resuspended in PBS.

The active compound is included in the pharmaceutically acceptable carrier in an amount sufficient to exert a therapeutically useful effect in the absence of undesirable side effects on the patient treated. The therapeutically effective concentration may be determined empirically by testing the compounds in *in vitro* and *in vivo* systems described herein and in International Patent Application Publication Nos. 99/27365 and 00/25134 (see, *e.g.*, EXAMPLES 53 and 54) and then extrapolated therefrom for dosages for humans.

The concentration of active compound in the pharmaceutical composition will depend on absorption, inactivation and excretion rates of the active compound, the physicochemical characteristics of the compound, the dosage schedule, and amount administered as well as other factors known to those of skill in the art. For example, the amount that is delivered is sufficient to ameliorate one or more of the symptoms of diseases or disorders associated with nuclear receptor activity or in which nuclear receptor activity is implicated, as described herein.

Typically a therapeutically effective dosage should produce a serum concentration of active ingredient of from about 0.1 ng/ml to about 50-100 μg/ml. The pharmaceutical compositions typically should provide a dosage of from about 0.001 mg to about 2000 mg of compound per kilogram of body weight per day. Pharmaceutical dosage unit forms are prepared to provide from about 1 mg to about 1000 mg and preferably from about 10 to about 500 mg of the essential active ingredient or a combination of essential ingredients per dosage unit form.

The active ingredient may be administered at once, or may be divided into a number of smaller doses to be administered at intervals of time. It is understood that the precise dosage and duration of treatment is a function of the disease being treated and may be determined empirically using known testing protocols or by extrapolation from *in vivo* or *in vitro* test data. It is to be noted that concentrations and dosage values may also vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that the concentration ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed compositions.

Pharmaceutically acceptable derivatives include acids, bases, enol ethers and esters, salts, esters, hydrates, solvates and prodrug forms.

The derivative is selected such that its pharmacokinetic properties are superior to the corresponding neutral compound.

Thus, effective concentrations or amounts of one or more of the compounds described herein or pharmaceutically acceptable derivatives thereof are mixed with a suitable pharmaceutical carrier or vehicle for systemic, topical or local administration to form pharmaceutical compositions. Compounds are included in an amount effective for ameliorating one or more symptoms of, or for treating or preventing diseases or disorders associated with nuclear receptor activity or in which nuclear receptor activity is implicated, as described herein. The concentration of active compound in the composition will depend on absorption, inactivation, excretion rates of the active compound, the dosage schedule, amount administered, particular formulation as well as other factors known to those of skill in the art.

The compositions are intended to be administered by a suitable route, including orally, parenterally, rectally, topically and locally. For oral administration, capsules and tablets are presently preferred. The compositions are in liquid, semi-liquid or solid form and are formulated in a manner suitable for each route of administration. Preferred modes of administration include parenteral and oral modes of administration. Oral administration is presently most preferred.

Solutions or suspensions used for parenteral, intradermal, subcutaneous, or topical application can include any of the following components: a sterile diluent, such as water for injection, saline solution, fixed oil, polyethylene glycol, glycerine, propylene glycol or other synthetic solvent; antimicrobial agents, such as benzyl alcohol and methyl parabens; antioxidants, such as ascorbic acid and sodium bisulfite; chelating agents, such as ethylenediaminetetraacetic acid (EDTA); buffers, such as acetates, citrates and phosphates; and agents for the adjustment of tonicity such as sodium chloride or dextrose. Parenteral

preparations can be enclosed in ampules, disposable syringes or single or multiple dose vials made of glass, plastic or other suitable material.

In instances in which the compounds exhibit insufficient solubility, methods for solubilizing compounds may be used. Such methods are known to those of skill in this art, and include, but are not limited to, using cosolvents, such as dimethylsulfoxide (DMSO), using surfactants, such as TWEEN®, or dissolution in aqueous sodium bicarbonate. Derivatives of the compounds, such as prodrugs of the compounds may also be used in formulating effective pharmaceutical compositions.

Upon mixing or addition of the compound(s), the resulting mixture may be a solution, suspension, emulsion or the like. The form of the resulting mixture depends upon a number of factors, including the intended mode of administration and the solubility of the compound in the selected carrier or vehicle. The effective concentration is sufficient for ameliorating the symptoms of the disease, disorder or condition treated and may be empirically determined.

The pharmaceutical compositions are provided for administration to humans and animals in unit dosage forms, such as tablets, capsules, pills, powders, granules, sterile parenteral solutions or suspensions, and oral solutions or suspensions, and oil-water emulsions containing suitable quantities of the compounds or pharmaceutically acceptable derivatives thereof. The pharmaceutically therapeutically active compounds and derivatives thereof are typically formulated and administered in unit-dosage forms or multiple-dosage forms. Unit-dose forms as used herein refers to physically discrete units suitable for human and animal subjects and packaged individually as is known in the art. Each unit-dose contains a predetermined quantity of the therapeutically active compound sufficient to produce the desired therapeutic effect, in association with the required pharmaceutical carrier, vehicle or diluent. Examples of unit-dose forms include ampoules and syringes and individually packaged tablets or capsules. Unit-dose forms may be administered in fractions or

multiples thereof. A multiple-dose form is a plurality of identical unit-dosage forms packaged in a single container to be administered in segregated unit-dose form. Examples of multiple-dose forms include vials, bottles of tablets or capsules or bottles of pints or gallons. Hence, multiple dose form is a multiple of unit-doses which are not segregated in packaging.

The composition can contain along with the active ingredient: a diluent such as lactose, sucrose, dicalcium phosphate, or carboxymethyl-cellulose; a lubricant, such as magnesium stearate, calcium stearate and talc; and a binder such as starch, natural gums, such as gum acacia-gelatin, glucose, molasses, polvinylpyrrolidine, celluloses and derivatives thereof, povidone, crospovidones and other such binders known to those of skill in the art. Liquid pharmaceutically administrable compositions can, for example, be prepared by dissolving, dispersing, or otherwise mixing an active compound as defined above and optional pharmaceutical adjuvants in a carrier, such as, for example, water, saline, aqueous dextrose, glycerol, glycols, ethanol, and the like, to thereby form a solution or suspension. If desired, the pharmaceutical composition to be administered may also contain minor amounts of nontoxic auxiliary substances such as wetting agents, emulsifying agents, or solubilizing agents, pH buffering agents and the like, for example, acetate, sodium citrate, cyclodextrine derivatives, sorbitan monolaurate, triethanolamine sodium acetate, triethanolamine oleate, and other such agents. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, Pa., 15th Edition, 1975. The composition or formulation to be administered will, in any event, contain a quantity of the active compound in an amount sufficient to alleviate the symptoms of the treated subject.

Dosage forms or compositions containing active ingredient in the range of 0.005% to 100% with the balance made up from non-toxic

carrier may be prepared. For oral administration, a pharmaceutically acceptable non-toxic composition is formed by the incorporation of any of the normally employed excipients, such as, for example pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, talcum, cellulose derivatives, sodium crosscarmellose, glucose, sucrose, magnesium carbonate or sodium saccharin. Such compositions include solutions, suspensions, tablets, capsules, powders and sustained release formulations, such as, but not limited to, implants and microencapsulated delivery systems, and biodegradable, biocompatible polymers, such as collagen, ethylene vinyl acetate, polyanhydrides, polyglycolic acid, polyorthoesters, polylactic acid and others. Methods for preparation of these compositions are known to those skilled in the art. The contemplated compositions may contain 0.001%-100% active ingredient, preferably 0.1-85%, typically 75-95%.

The active compounds or pharmaceutically acceptable derivatives may be prepared with carriers that protect the compound against rapid elimination from the body, such as time release formulations or coatings.

The compositions may include other active compounds to obtain desired combinations of properties. The compounds provided herein, or pharmaceutically acceptable derivatives thereof as described herein, may also be advantageously administered for therapeutic or prophylactic purposes together with another pharmacological agent known in the general art to be of value in treating one or more of the diseases or medical conditions referred to hereinabove, such as diseases or disorders associated with nuclear receptor activity or in which nuclear receptor activity is implicated. It is to be understood that such combination therapy constitutes a further aspect of the compositions and methods of treatment provided herein.

1. **Compositions for oral administration**

Oral pharmaceutical dosage forms are either solid, gel or liquid. The solid dosage forms are tablets, capsules, granules, and bulk powders. Types of oral tablets include compressed, chewable lozenges and tablets which may be enteric-coated, sugar-coated or film-coated. Capsules may be hard or soft gelatin capsules, while granules and powders may be provided in non-effervescent or effervescent form with the combination of other ingredients known to those skilled in the art.

In certain embodiments, the formulations are solid dosage forms, preferably capsules or tablets. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder; a diluent; a disintegrating agent; a lubricant; a glidant; a sweetening agent; and a flavoring agent.

Examples of binders include microcrystalline cellulose, gum tragacanth, glucose solution, acacia mucilage, gelatin solution, sucrose and starch paste. Lubricants include talc, starch, magnesium or calcium stearate, lycopodium and stearic acid. Diluents include, for example, lactose, sucrose, starch, kaolin, salt, mannitol and dicalcium phosphate. Glidants include, but are not limited to, colloidal silicon dioxide. Disintegrating agents include crosscarmellose sodium, sodium starch glycolate, alginic acid, corn starch, potato starch, bentonite, methylcellulose, agar and carboxymethylcellulose. Coloring agents include, for example, any of the approved certified water soluble FD and C dyes, mixtures thereof; and water insoluble FD and C dyes suspended on alumina hydrate. Sweetening agents include sucrose, lactose, mannitol and artificial sweetening agents such as saccharin, and any number of spray dried flavors. Flavoring agents include natural flavors extracted from plants such as fruits and synthetic blends of compounds which produce a pleasant sensation, such as, but not limited to peppermint and methyl salicylate. Wetting agents include propylene glycol monostearate, sorbitan monooleate, diethylene glycol monolaurate and polyoxyethylene

laural ether. Emetic-coatings include fatty acids, fats, waxes, shellac, ammoniated shellac and cellulose acetate phthalates. Film coatings include hydroxyethylcellulose, sodium carboxymethylcellulose, polyethylene glycol 4000 and cellulose acetate phthalate.

If oral administration is desired, the compound could be provided in a composition that protects it from the acidic environment of the stomach. For example, the composition can be formulated in an enteric coating that maintains its integrity in the stomach and releases the active compound in the intestine. The composition may also be formulated in combination with an antacid or other such ingredient.

When the dosage unit form is a capsule, it can contain, in addition to material of the above type, a liquid carrier such as a fatty oil. In addition, dosage unit forms can contain various other materials which modify the physical form of the dosage unit, for example, coatings of sugar and other enteric agents. The compounds can also be administered as a component of an elixir, suspension, syrup, wafer, sprinkle, chewing gum or the like. A syrup may contain, in addition to the active compounds, sucrose as a sweetening agent and certain preservatives, dyes and colorings and flavors.

The active materials can also be mixed with other active materials which do not impair the desired action, or with materials that supplement the desired action, such as antacids, H2 blockers, and diuretics. The active ingredient is a compound or pharmaceutically acceptable derivative thereof as described herein. Higher concentrations, up to about 98% by weight of the active ingredient may be included.

Pharmaceutically acceptable carriers included in tablets are binders, lubricants, diluents, disintegrating agents, coloring agents, flavoring agents, and wetting agents. Enteric-coated tablets, because of the enteric-coating, resist the action of stomach acid and dissolve or disintegrate in the neutral or alkaline intestines. Sugar-coated tablets are compressed tablets to which different layers of pharmaceutically

acceptable substances are applied. Film-coated tablets are compressed tablets which have been coated with a polymer or other suitable coating. Multiple compressed tablets are compressed tablets made by more than one compression cycle utilizing the pharmaceutically acceptable substances previously mentioned. Coloring agents may also be used in the above dosage forms. Flavoring and sweetening agents are used in compressed tablets, sugar-coated, multiple compressed and chewable tablets. Flavoring and sweetening agents are especially useful in the formation of chewable tablets and lozenges.

Liquid oral dosage forms include aqueous solutions, emulsions, suspensions, solutions and/or suspensions reconstituted from non-effervescent granules and effervescent preparations reconstituted from effervescent granules. Aqueous solutions include, for example, elixirs and syrups. Emulsions are either oil-in-water or water-in-oil.

Elixirs are clear, sweetened, hydroalcoholic preparations. Pharmaceutically acceptable carriers used in elixirs include solvents. Syrups are concentrated aqueous solutions of a sugar, for example, sucrose, and may contain a preservative. An emulsion is a two-phase system in which one liquid is dispersed in the form of small globules throughout another liquid. Pharmaceutically acceptable carriers used in emulsions are non-aqueous liquids, emulsifying agents and preservatives. Suspensions use pharmaceutically acceptable suspending agents and preservatives. Pharmaceutically acceptable substances used in non-effervescent granules, to be reconstituted into a liquid oral dosage form, include diluents, sweeteners and wetting agents. Pharmaceutically acceptable substances used in effervescent granules, to be reconstituted into a liquid oral dosage form, include organic acids and a source of carbon dioxide. Coloring and flavoring agents are used in all of the above dosage forms.

Solvents include glycerin, sorbitol, ethyl alcohol and syrup. Examples of preservatives include glycerin, methyl and propylparaben,

benzoic add, sodium benzoate and alcohol. Examples of non-aqueous liquids utilized in emulsions include mineral oil and cottonseed oil. Examples of emulsifying agents include gelatin, acacia, tragacanth, bentonite, and surfactants such as polyoxyethylene sorbitan monooleate. Suspending agents include sodium carboxymethylcellulose, pectin, tragacanth, Veegum and acacia. Diluents include lactose and sucrose. Sweetening agents include sucrose, syrups, glycerin and artificial sweetening agents such as saccharin. Wetting agents include propylene glycol monostearate, sorbitan monooleate, diethylene glycol monolaurate and polyoxyethylene lauryl ether. Organic adds include citric and tartaric acid. Sources of carbon dioxide include sodium bicarbonate and sodium carbonate. Coloring agents include any of the approved certified water soluble FD and C dyes, and mixtures thereof. Flavoring agents include natural flavors extracted from plants such fruits, and synthetic blends of compounds which produce a pleasant taste sensation.

For a solid dosage form, the solution or suspension, in for example propylene carbonate, vegetable oils or triglycerides, is preferably encapsulated in a gelatin capsule. Such solutions, and the preparation and encapsulation thereof, are disclosed in U.S. Patent Nos 4,328,245; 4,409,239; and 4,410,545. For a liquid dosage form, the solution, *e.g.*, for example, in a polyethylene glycol, may be diluted with a sufficient quantity of a pharmaceutically acceptable liquid carrier, *e.g.*, water, to be easily measured for administration.

Alternatively, liquid or semi-solid oral formulations may be prepared by dissolving or dispersing the active compound or salt in vegetable oils, glycols, triglycerides, propylene glycol esters (*e.g.*, propylene carbonate) and other such carriers, and encapsulating these solutions or suspensions in hard or soft gelatin capsule shells. Other useful formulations include those set forth in U.S. Patent Nos. Re 28,819 and 4,358,603. Briefly, such formulations include, but are not limited to, those containing a compound provided herein, a dialkylated mono- or poly-alkylene glycol,

including, but not limited to, 1,2-dimethoxymethane, diglyme, triglyme, tetraglyme, polyethylene glycol-350-dimethyl ether, polyethylene glycol-550-dimethyl ether, polyethylene glycol-750-dimethyl ether wherein 350, 550 and 750 refer to the approximate average molecular weight of the polyethylene glycol, and one or more antioxidants, such as butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), propyl gallate, vitamin E, hydroquinone, hydroxycoumarins, ethanolamine, lecithin, cephalin, ascorbic acid, malic acid, sorbitol, phosphoric acid, thiodipropionic acid and its esters, and dithiocarbamates.

Other formulations include, but are not limited to, aqueous alcoholic solutions including a pharmaceutically acceptable acetal. Alcohols used in these formulations are any pharmaceutically acceptable water-miscible solvents having one or more hydroxyl groups, including, but not limited to, propylene glycol and ethanol. Acetals include, but are not limited to, di(lower alkyl) acetals of lower alkyl aldehydes such as acetaldehyde diethyl acetal.

In all embodiments, tablets and capsules formulations may be coated as known by those of skill in the art in order to modify or sustain dissolution of the active ingredient. Thus, for example, they may be coated with a conventional enterically digestible coating, such as phenylsalicylate, waxes and cellulose acetate phthalate.

2. Injectables, solutions and emulsions

Parenteral administration, generally characterized by injection, either subcutaneously, intramuscularly or intravenously is also contemplated herein. Injectables can be prepared in conventional forms, either as liquid solutions or suspensions, solid forms suitable for solution or suspension in liquid prior to injection, or as emulsions. Suitable excipients are, for example, water, saline, dextrose, glycerol or ethanol. In addition, if desired, the pharmaceutical compositions to be administered may also contain minor amounts of non-toxic auxiliary substances such as wetting or emulsifying agents, pH buffering agents,

stabilizers, solubility enhancers, and other such agents, such as for example, sodium acetate, sorbitan monolaurate, triethanolamine oleate and cyclodextrins. Implantation of a slow-release or sustained-release system, such that a constant level of dosage is maintained (see, *e.g.*, U.S. Patent No. 3,710,795) is also contemplated herein. Briefly, a compound provided herein is dispersed in a solid inner matrix, *e.g.*, polymethylmethacrylate, polybutylmethacrylate, plasticized or unplasticized polyvinylchloride, plasticized nylon, plasticized polyethyleneterephthalate, natural rubber, polyisoprene, polyisobutylene, polybutadiene, polyethylene, ethylene-vinylacetate copolymers, silicone rubbers, polydimethylsiloxanes, silicone carbonate copolymers, hydrophilic polymers such as hydrogels of esters of acrylic and methacrylic acid, collagen, cross-linked polyvinylalcohol and cross-linked partially hydrolyzed polyvinyl acetate, that is surrounded by an outer polymeric membrane, *e.g.*, polyethylene, polypropylene, ethylene/propylene copolymers, ethylene/ethyl acrylate copolymers, ethylene/vinylacetate copolymers, silicone rubbers, polydimethyl siloxanes, neoprene rubber, chlorinated polyethylene, polyvinylchloride, vinylchloride copolymers with vinyl acetate, vinylidene chloride, ethylene and propylene, ionomer polyethylene terephthalate, butyl rubber epichlorohydrin rubbers, ethylene/vinyl alcohol copolymer, ethylene/vinyl acetate/vinyl alcohol terpolymer, and ethylene/vinyloxyethanol copolymer, that is insoluble in body fluids. The compound diffuses through the outer polymeric membrane in a release rate controlling step. The percentage of active compound contained in such parenteral compositions is highly dependent on the specific nature thereof, as well as the activity of the compound and the needs of the subject.

Parenteral administration of the compositions includes intravenous, subcutaneous and intramuscular administrations. Preparations for parenteral administration include sterile solutions ready for injection, sterile dry soluble products, such as lyophilized powders, ready to be

combined with a solvent just prior to use, including hypodermic tablets, sterile suspensions ready for injection, sterile dry insoluble products ready to be combined with a vehicle just prior to use and sterile emulsions. The solutions may be either aqueous or nonaqueous.

If administered intravenously, suitable carriers include physiological saline or phosphate buffered saline (PBS), and solutions containing thickening and solubilizing agents, such as glucose, polyethylene glycol, and polypropylene glycol and mixtures thereof.

Pharmaceutically acceptable carriers used in parenteral preparations include aqueous vehicles, nonaqueous vehicles, antimicrobial agents, isotonic agents, buffers, antioxidants, local anesthetics, suspending and dispersing agents, emulsifying agents, sequestering or chelating agents and other pharmaceutically acceptable substances.

Examples of aqueous vehicles include Sodium Chloride Injection, Ringers Injection, Isotonic Dextrose Injection, Sterile Water Injection, Dextrose and Lactated Ringers Injection. Nonaqueous parenteral vehicles include fixed oils of vegetable origin, cottonseed oil, corn oil, sesame oil and peanut oil. Antimicrobial agents in bacteriostatic or fungistatic concentrations must be added to parenteral preparations packaged in multiple-dose containers which include phenols or cresols, mercurials, benzyl alcohol, chlorobutanol, methyl and propyl p-hydroxybenzoic acid esters, thimerosal, benzalkonium chloride and benzethonium chloride. Isotonic agents include sodium chloride and dextrose. Buffers include phosphate and citrate. Antioxidants include sodium bisulfate. Local anesthetics include procaine hydrochloride. Suspending and dispersing agents include sodium carboxymethylcelluose, hydroxypropyl methylcellulose and polyvinylpyrrolidone. Emulsifying agents include Polysorbate 80 (TWEEN® 80). A sequestering or chelating agent of metal ions include EDTA. Pharmaceutical carriers also include ethyl alcohol, polyethylene glycol and propylene glycol for water miscible vehicles and

sodium hydroxide, hydrochloric acid, citric acid or lactic acid for pH adjustment.

The concentration of the pharmaceutically active compound is adjusted so that an injection provides an effective amount to produce the desired pharmacological effect. The exact dose depends on the age, weight and condition of the patient or animal as is known in the art.

The unit-dose parenteral preparations are packaged in an ampoule, a vial or a syringe with a needle. All preparations for parenteral administration must be sterile, as is known and practiced in the art.

Illustratively, intravenous or intraarterial infusion of a sterile aqueous solution containing an active compound is an effective mode of administration. Another embodiment is a sterile aqueous or oily solution or suspension containing an active material injected as necessary to produce the desired pharmacological effect.

Injectables are designed for local and systemic administration. Typically a therapeutically effective dosage is formulated to contain a concentration of at least about 0.1% w/w up to about 90% w/w or more, preferably more than 1% w/w of the active compound to the treated tissue(s). The active ingredient may be administered at once, or may be divided into a number of smaller doses to be administered at intervals of time. It is understood that the precise dosage and duration of treatment is a function of the tissue being treated and may be determined empirically using known testing protocols or by extrapolation from *in vivo* or *in vitro* test data. It is to be noted that concentrations and dosage values may also vary with the age of the individual treated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the formulations, and that the concentration ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed formulations.

The compound may be suspended in micronized or other suitable form or may be derivatized to produce a more soluble active product or to produce a prodrug. The form of the resulting mixture depends upon a number of factors, including the intended mode of administration and the solubility of the compound in the selected carrier or vehicle. The effective concentration is sufficient for ameliorating the symptoms of the condition and may be empirically determined.

3. Lyophilized powders

Of interest herein are also lyophilized powders, which can be reconstituted for administration as solutions, emulsions and other mixtures. They may also be reconstituted and formulated as solids or gels.

The sterile, lyophilized powder is prepared by dissolving a compound provided herein, or a pharmaceutically acceptable derivative thereof, in a suitable solvent. The solvent may contain an excipient which improves the stability or other pharmacological component of the powder or reconstituted solution, prepared from the powder. Excipients that may be used include, but are not limited to, dextrose, sorbital, fructose, corn syrup, xylitol, glycerin, glucose, sucrose or other suitable agent. The solvent may also contain a buffer, such as citrate, sodium or potassium phosphate or other such buffer known to those of skill in the art at, typically, about neutral pH. Subsequent sterile filtration of the solution followed by lyophilization under standard conditions known to those of skill in the art provides the desired formulation. Generally, the resulting solution will be apportioned into vials for lyophilization. Each vial will contain a single dosage (10-1000 mg, preferably 100-500 mg) or multiple dosages of the compound. The lyophilized powder can be stored under appropriate conditions, such as at about 4 °C to room temperature.

Reconstitution of this lyophilized powder with water for injection provides a formulation for use in parenteral administration. For reconstitution, about 1-50 mg, preferably 5-35 mg, more preferably about

9-30 mg of lyophilized powder, is added per mL of sterile water or other suitable carrier. The precise amount depends upon the selected compound. Such amount can be empirically determined.

4. Topical administration

Topical mixtures are prepared as described for the local and systemic administration. The resulting mixture may be a solution, suspension, emulsions or the like and are formulated as creams, gels, ointments, emulsions, solutions, elixirs, lotions, suspensions, tinctures, pastes, foams, aerosols, irrigations, sprays, suppositories, bandages, dermal patches or any other formulations suitable for topical administration.

The compounds or pharmaceutically acceptable derivatives thereof may be formulated as aerosols for topical application, such as by inhalation (see, *e.g.*, U.S. Patent Nos. 4,044,126, 4,414,209, and 4,364,923, which describe aerosols for delivery of a steroid useful for treatment of inflammatory diseases, particularly asthma). These formulations for administration to the respiratory tract can be in the form of an aerosol or solution for a nebulizer, or as a microfine powder for insufflation, alone or in combination with an inert carrier such as lactose. In such a case, the particles of the formulation will typically have diameters of less than 50 microns, preferably less than 10 microns.

The compounds may be formulated for local or topical application, such as for topical application to the skin and mucous membranes, such as in the eye, in the form of gels, creams, and lotions and for application to the eye or for intracisternal or intraspinal application. Topical administration is contemplated for transdermal delivery and also for administration to the eyes or mucosa, or for inhalation therapies. Nasal solutions of the active compound alone or in combination with other pharmaceutically acceptable excipients can also be administered.

These solutions, particularly those intended for ophthalmic use, may be formulated as 0.01% - 10% isotonic solutions, pH about 5-7, with appropriate salts.

5. Compositions for other routes of administration

Other routes of administration, such as topical application, transdermal patches, and rectal administration are also contemplated herein.

For example, pharmaceutical dosage forms for rectal administration are rectal suppositories, capsules and tablets for systemic effect. Rectal suppositories are used herein mean solid bodies for insertion into the rectum which melt or soften at body temperature releasing one or more pharmacologically or therapeutically active ingredients. Pharmaceutically acceptable substances utilized in rectal suppositories are bases or vehicles and agents to raise the melting point. Examples of bases include cocoa butter (theobroma oil), glycerin-gelatin, carbowax (polyoxyethylene glycol) and appropriate mixtures of mono-, di- and triglycerides of fatty acids. Combinations of the various bases may be used. Agents to raise the melting point of suppositories include spermaceti and wax. Rectal suppositories may be prepared either by the compressed method or by molding. The typical weight of a rectal suppository is about 2 to 3 gm.

Tablets and capsules for rectal administration are manufactured using the same pharmaceutically acceptable substance and by the same methods as for formulations for oral administration.

6. Articles of manufacture

The compounds or pharmaceutically acceptable derivatives may be packaged as articles of manufacture containing packaging material, a compound or pharmaceutically acceptable derivative thereof provided herein, which is effective for modulating the activity of nuclear receptors, including FXR and/or orphan nuclear receptors, or for treatment, prevention or amelioration of one or more symptoms of nuclear receptor, including FXR and/or orphan nuclear receptor, mediated diseases or

disorders, or diseases or disorders in which nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, is implicated, within the packaging material, and a label that indicates that the compound or composition, or pharmaceutically acceptable derivative thereof, is used for modulating the activity of nuclear receptors, including FXR and/or orphan nuclear receptors, or for treatment, prevention or amelioration of one or more symptoms of nuclear receptor, including FXR and/or orphan nuclear receptor, mediated diseases or disorders, or diseases or disorders in which nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, is implicated.

The articles of manufacture provided herein contain packaging materials. Packaging materials for use in packaging pharmaceutical products are well known to those of skill in the art. See, *e.g.*, U.S. Patent Nos. 5,323,907, 5,052,558 and 5,033,252. Examples of pharmaceutical packaging materials include, but are not limited to, blister packs, bottles, tubes, inhalers, pumps, bags, vials, containers, syringes, bottles, and any packaging material suitable for a selected formulation and intended mode of administration and treatment. A wide array of formulations of the compounds and compositions provided herein are contemplated as are a variety of treatments for any disease or disorder in which nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, is implicated as a mediator or contributor to the symptoms or cause.

E. Evaluation of the activity of the compounds

Standard physiological, pharmacological and biochemical procedures are available for testing the compounds to identify those that possess biological activities that modulate the activity or nuclear receptors, including FXR and/or orphan nuclear receptors. Such assays are disclosed in International Patent Application Publication Nos. WO 99/27365 and WO 00/25134.

Briefly, in one assay, a nuclear hormone receptor, a peptide sensor that provides direct, *in vitro* binding to the receptor under the assay conditions, and a compound provided herein are combined. The modulation of the binding of the sensor to the receptor is measured and compared to control. Generally, the sensor is a peptide containing a fluorescent label, such as rhodanine. The assay is typically performed in a buffer solution, but may be performed in a solid phase format.

In another assay, the ability of the compounds provided herein to mediate the heterodimerization between purified bacterial expressed FXR with RXRα ligand binding domains (LBD) is measured. Detection of the associated LBD's are measured by time resolved fluorimetry (TRF). The purified LBD of FXR is labeled with biotin then mixed with stoichiometric amounts of europium labeled streptavidin (Wallac Inc.). The purified LBD of RXRα is labeled with CY5™. Equimolar amounts of each modified LBD are mixed together and allowed to equilibrate for at least 1 hour prior to addition to either variable or constant concentrations of the sample for which the affinity is to be determined. After equilibration, the time-resolved fluorescent signal is quantitated using a fluorescent plate reader. The affinity of the compound is estimated from a plot of fluorescence versus concentration of compound added.

Another assay is a Time Resolved Fluorescence Resonance Energy Transfer (TR-FRET) assay. The ability of FXR ligands to promote protein-protein interactions between the ligand binding domain (LBD) of FXR and transcriptional coactivator proteins can be exploited to measure the FXR agonist or antagonist activity of compounds. TR-FRET relies upon the transfer of energy from a donor molecule to an acceptor molecule that only occurs when donor and acceptor are in close proximity. In practice, the FXR TR-FRET assay uses a recombinant Glutathione-S-transferase (GST)-FXR LBD fusion protein and a synthetic biotinylated peptide sequenced derived from the receptor interacting domain of the steroid receptor coactivator 1 (SRC-1). In the case of FXR, the human FXR LBD

(amino acids 244 to 472) was cloned in to pGEX vector and the resultant GST-FXR-LBD protein was expressed in DH5α and purified on glutathione beads. The FXR-LBD is labeled with a europium chelate (donor) via a europium-tagged anti-GST antibody. The peptide is labeled with allophycocyanin via a streptavidin-biotin linkage.

In the presence of an FXR agonist, the peptide is recruited to the GST-FXR-LBD bringing europium and allophycocyanin into close proximity. Upon excitation of the reaction at 340 nm the Europium chelate emits at 615 nm, exciting the allophycocyanin, resulting in emission at 665 nm. The reading at 665 nm gives an indication of the strength of the protein-protein interaction. The activity of an FXR antagonist can be measured by determining the ability of a compound to competitively inhibit (*i.e.*, IC_{50}) the activity of an FXR agonist.

Further assays for use herein are cell-based assays, including an FXR co-transfection assay. To measure the ability of FXR ligands to activate or inhibit the transcriptional activity of FXR, a cell-based cotransfection assay is used. It has been shown that FXR functions as a heterodimer with RXR. For the co-transfection assay, expression plasmids for FXR and RXR are introduced via transient transfection into mammalian cells along with a luciferase reporter plasmid that contains seven copies of a DNA sequence that is bound by FXR-RXR heterodimers (Ecdysone receptor response element or ECRE). Treatment of transfected cells with an FXR agonist increases the transcriptional activity of FXR which is measure by an increase in luciferase activity. Similarly, FXR antagonist activity can be measured by determining the ability of a compound to competitively inhibit the activity of a FXR agonist.

F. Methods of use of the compounds and compositions

Methods of use of the compounds and compositions provided herein are also provided. The methods involve both *in vitro* and *in vivo* uses of the compounds and compositions for altering nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, and for

treatment, prevention, or amelioration of one or more symptoms of diseases or disorder that are modulated by nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, or in which nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, is implicated.

Methods of reducing cholesterol levels and of modulating cholesterol metabolism are provided. As described above, FXR is implicated in modulating cholesterol metabolism, catabolism and absorption of dietary cholesterol. See, *e.g.*, International Patent Application Publication No. 00/40965.

Method of altering nuclear receptor activity, including FXR and/or orphan nuclear receptor activity, by contacting the receptor with one or more compounds or compositions provided herein, are provided.

Methods of treatment, prevention, or amelioration of one or more symptoms of a disease or disorder which is affected by cholesterol, triglyceride, or bile acid levels are provided.

Methods of treatment, prevention, or amelioration of one or more symptoms of hypercholesterolemia (see, *e.g.*, International Patent Application Publication No. WO 00/57915); hyperlipoproteinemia (see, *e.g.*, International Patent Application Publication No. WO 01/60818); hypertriglyceridemia, lipodystrophy, hyperglycemia or diabetes mellitus (see, *e.g.*, International Patent Application Publication No. WO 01/82917); dyslipidemia, obesity, atherosclerosis, lipid disorders, cardiovascular disorders, or gallstone disease (see, *e.g.*, International Patent Application Publication No. WO 00/37077); acne vulgaris or acneiform skin conditions (see, *e.g.*, International Patent Application Publication No. WO 00/49992); atherosclerosis, diabetes, Parkinson's disease, inflammation, immunological disorders, obesity, cancer or Alzheimer's disease (see, *e.g.*, International Patent Application Publication No. WO 00/17334); conditions characterized by a perturbed epidermal barrier function, hyperlipidemia, cholestasis, peripheral occlusive disease,

ischemic stroke, or conditions of disturbed differentiation or excess proliferation of the epidermis or mucous membrane (see, *e.g.*, U.S. Patent Nos. 6,184,215 and 6,187,814, and International Patent Application Publication No. WO 98/32444) are provided.

Methods of increasing cholesterol efflux from mammalian cells using the compounds and compositions provided herein are provided (see, *e.g.*, International Patent Application Publication No. WO 00/78972).

Methods of increasing the expression of ATP-Binding Cassette (ABC1) in mammalian cells using the compounds and compositions provided herein are provided (see, *e.g.*, International Patent Application Publication No. WO 00/78972).

Methods of treating, preventing, or ameliorating one or more symptoms of hypocholesterolemia using the compounds and compositions provided herein are also provided.

G. Combination Therapy

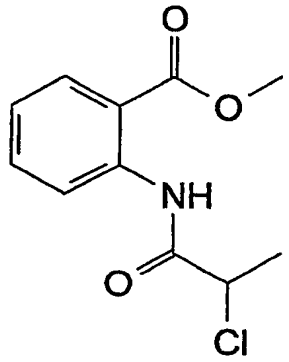
Also contemplated herein is combination therapy using a compound provided herein, or a pharmaceutically acceptable derivative thereof, in combination with one or more of the following: antihyperlipidemic agents, plasma HDL-raising agents, antihypercholesterolemic agents, cholesterol biosynthesis inhibitors (such as HMG CoA reductase inhibitors, such as lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin and rivastatin), acyl-coenzyme A:cholesterol acytransferase (ACAT) inhibitors, probucol, raloxifene, nicotinic acid, niacinamide, cholesterol absorption inhibitors, bile acid sequestrants (such as anion exchange resins, or quaternary amines (*e.g.*, cholestyramine or colestipol)), low density lipoprotein receptor inducers, clofibrate, fenofibrate, benzofibrate, cipofibrate, gemfibrizol, vitamin B_6, vitamin B_{12}, anti-oxidant vitamins, β-blockers, anti-diabetes agents, angiotensin II antagonists, angiotensin converting enzyme inhibitors, platelet aggregation inhibitors, fibrinogen receptor antagonists, aspirin or fibric acid derivatives. The compound provided herein, or pharmaceutically

acceptable derivative thereof, is administered simultaneously with, prior to, or after administration of one or more of the above agents. Pharmaceutical compositions containing a compound provided herein and one or more of the above agents are also provided.

The following examples are included for illustrative purposes only and are not intended to limit the scope of the invention. Starting materials in the synthesis examples below are either available from commercial sources or via literature procedures. All commercially available compounds were used without further purification unless otherwise indicated. $CDCl_3$ (99.8% D, Cambridge Isotope Laboratories) was used in all experiments as indicated. Proton (^1H) nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance 400 MHz NMR spectrometer. Significant peaks are tabulated and typically include: number of protons, multiplicity (s, singlet; d, double; t, triplet; q, quartet; m, multiplet; br s, broad singlet). Chemical shifts are reported as parts per million (δ) relative to tetramethylsilane. Low resolution mass spectra (MS) were obtained as electrospray ionization (ESI) mass spectra, which were recorded on a Perkin-Elmer SCIEX HPLC/MS instrument using reverse-phase conditions (acetonitrile/water, 0.05% trifluoroacetic acid). Flash chromatography was performed using Merck Silica Gel 60 (230-400 mesh) following standard protocol (Still et al. *J. Org. Chem.* **1978**, *43*, 2923).

EXAMPLE 1

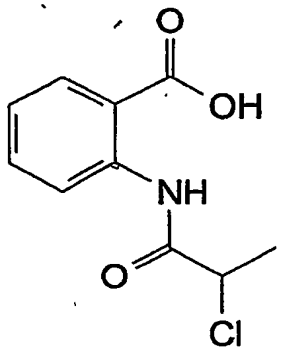
Preparation of 2-(2-Chloro-propionylamino)-benzoic acid methyl ester



To methyl anthranilate (5 g, 33.1 mmol) stirring in DCM at 0 °C under N_2 was added DIEA (5.1 g, 39.7 mmol) in one portion followed by the dropwise addition of 2-chloropropionyl chloride (4.2 g, 33.1 mmol). The reaction was allowed to stir at 0 °C for 30 min. then warmed to room temperature, stirring for an additional 3 h. The reaction was treated with saturated aqueous solution of $NaHCO_3$ and the resulting biphasic mixture transferred to a separatory funnel. The layers separated and the aqueous layer was extracted twice more with DCM (25 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum to afford the desired product (7.75 g, 97% yield), which was used without further purification. ^{1}H-NMR ($CDCl_3$): δ 11.8 (br, 1H), 8.72 (dd, 1H), 8.08 (dd, 1H), 7.58 (m, 1H), 7.15 (m, 1H), 4.56 (q, 1H), 3.97 (s, 3H), 1.85 (d, 3H).

EXAMPLE 2

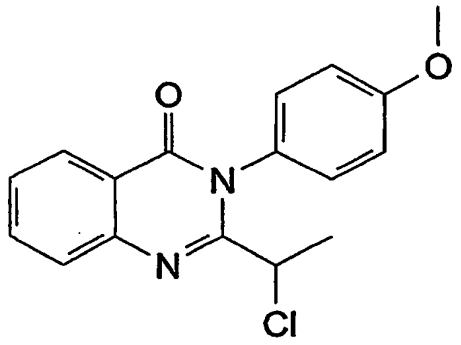
Preparation of 2-(2-Chloro-propionylamino)-benzoic acid



To the 2-(2-chloro-propionylamino)-benzoic acid methyl ester (7.75 g, 32.1 mmol) stirring in THF (40 mL) was added 1M $LiOH/H_2O$ (40 mL). The reaction was allowed to stir at 50 °C for 3 h. After this period the reaction was concentrated under vacuum to afford a crude residue that was acidified with 1N HCl. The resulting suspension was then diluted with EtOAc and washed with water (3 x 50 mL). The organic layer was then washed with brine (25 mL), dried over $MgSO_4$, and concentrated under vacuum to afford crude acid. The crude material was purified by flash chromatography (silica gel, 80% EtOAc/Hex) to afford the desired product as an off white solid (7.1 g, 97% yield). ^{1}H-NMR ($CDCl_3$): δ 8.6 (d, 1H), 8.12 (d, 1H), 7.61 (t, 1H), 7.57 (t, 1H), 4.89 (br, 1H), 4.65 (t, 1H), 1.78 (d, 3H).

EXAMPLE 3

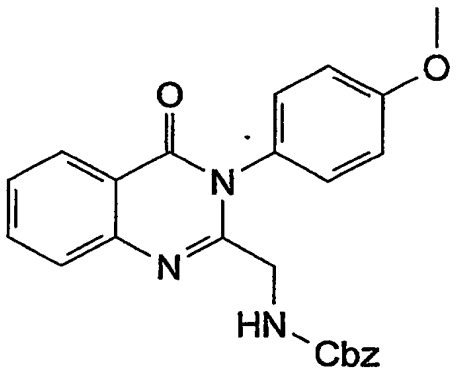
Preparation of 2-(1-Chloro-ethyl)-3-(4-methoxy-phenyl)-3H-quinazolin-4-one



To a stirring suspension of 2-(2-chloro-propionylamino)-benzoic acid (5 g, 22 mmol) and *p*-anisidine (2.7 g, 22 mmol) in 100 mL of toluene was added dropwise phosphorus trichloride (PCl_3) (3.02 g, 22 mmol) over 15 minutes. When the addition was complete the reaction was heated to reflux for 3 h and cooled to room temperature and treated with 5 mL water. The resulting mixture was concentrated under vacuum to yield a semi-solid residue that was treated with 1N HCl and extracted twice with 200 mL portions of EtOAc. The organic extracts were combined, washed with brine, dried over $MgSO_4$, and concentrated under vacuum to afford crude product that was purified by column chromatography (silica gel, EtOAc/Hex 4:1) (4.96 g, 72 % yield). ^{1}H-NMR ($CDCl_3$): δ 8.31 (m, 1H), 7.82 (m, 2H), 7.54 (m, 1H), 7.43 (dd, 1H), 7.09 (m, 3H), 4.66 (q, 1H), 3.91 (s, 3H), 1.89 (d, 3H).

EXAMPLE 4

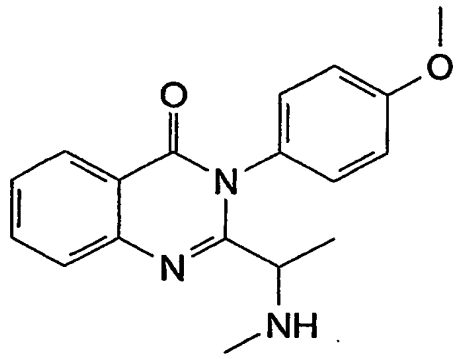
Preparation of [3-(4-Methoxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-ylmethyl]-carbamic acid benzyl ester



To a stirring suspension of 2-(2-benzyloxycarbonylamino-acetylamino)-benzoic acid (2 g, 6.1 mmol) in THF (100 mL) was added carbonyldiimidizole (CDI) (1.0 g, 6.2 mmol) and stirred for 1h at rt under a nitrogen atmosphere. After 1h the reaction was treated with *p*-anisidine (0.73 g, 6.1 mmol) and refluxed for 16 h. The reaction was cooled to room temperature and concentrated under vacuum to afford a crude residue that was dissolved in EtOAc (50 mL). The mixture was then washed with saturated $NaHCO_3$ (50 mL) followed with brine (25 mL). The organic layer was dried over $MgSO_4$ and concentrated under vacuum to afford crude product that was purified by flash chromatography (silica gel, EtOAc/Hex 4:1) (1.21 g, 48 % yield). ^{1}H-NMR ($CDCl_3$): δ 8.26 (m, 1H), 7.72(m, 2H), 7.47 (m, 1H), 7.34 (m, 5H), 7.19 (m, 2H), 7.03 (m, 2H), 6.28 (broad, 1H), 5.10 (s, 2H), 4.50 (s, 2H), 3.85 (s, 3H).

EXAMPLE 5

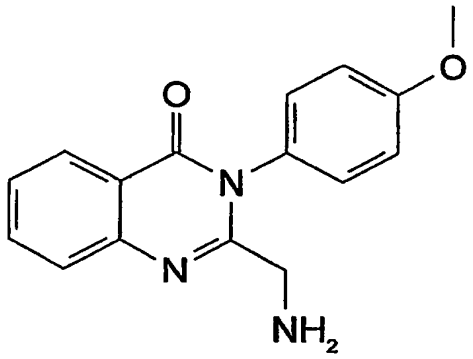
Preparation of 3-(4-Methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one



To the neat 2-(1-chloro-ethyl)-3-(4-methoxy-phenyl)-3H-quinazolin-4-one (1.0 g, 3.2 mmol) in a sealed tube was added 40 mL of a methylamine solution (1M in THF, 40 mmol). The tube was sealed and heated to 110 °C 16 h. The resulting solution was cooled to room temperature and concentrated under vacuum to afford the crude product that was purified by flash chromatography (5% MeOH/DCM, silica gel) (yield 0.97 g, 99%). ^{1}H-NMR (CD_3OD): δ 8.28 (m, 1H), 7.93 (m, 1H), 7.86 (m, 1H), 7.65 (m, 1H), 7.43 (m, 1H) 7.33 (m, 1H), 7.19 (m, 2H), 4.09 (q, 1H), 3.92 (s, 3H), 2.75 (s, 3H), 1.51 (d, 3H).

EXAMPLE 6

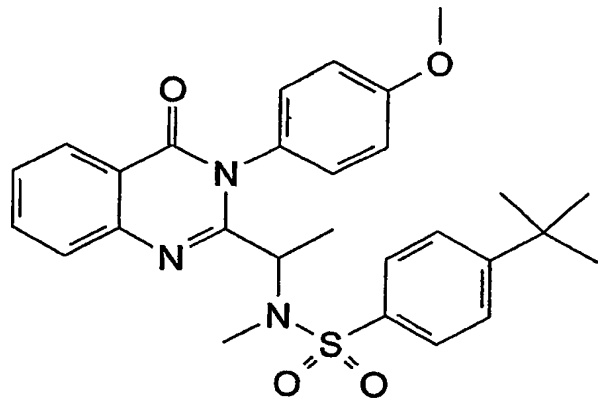
Preparation of 2-Aminomethyl-3-(4-methoxy-phenyl)-3H-quinazolin-4-one



In an oven dried flask that was purged with nitrogen was place 2-(2-benzyloxycarbonylamino-acetylamino)-benzoic acid (1.0 g, 2.4 mmol). The starting material was diluted with nitrogen sparged EtOH (25 mL) while maintaining a nitrogen atmosphere. To the reaction mixture was added 10% Pd/C (150 mg) and the reaction sealed with a septum. The sealed reaction was then purged with hydrogen by placing a syringe equipped with a balloon full of hydrogen gas through the septum. The reaction was stirred vigorously while inserting an additional needle in the septa to flush the atmosphere with hydrogen. With a full balloon of hydrogen in place the reaction was allowed to stir for 3 h after which it was concentrated under vacuum to yield crude material that was purified by flash chromatography (silica gel, 10% MeOH/DCM) (yield 0.67 g, 100 %). ^{1}H-NMR (CD_3OD): δ 8.23 (m, 1H), 7.87 (m, 1H), 7.80 (m, 1H), 7.56 (m, 1H), 7.13 (m, 2H), 7.01 (m, 2H), 3.90 (s, 3H), 3.51 (s, 2H); MS (ESI) 282 (MH^+).

EXAMPLE 7

Preparation of 4-tert-Butyl-N-{1-[3-(4-methoxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide

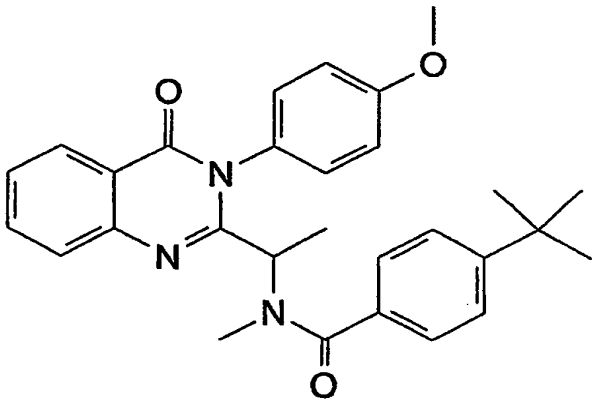


To a suspension of the 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one (50 mg, 0.16 mmol) stirring in 2 mL DCM was added TEA (19 mg, 0.19 mmol) followed by the addition of neat 4-tert-butyl-benzenesulfonyl chloride (37 mg, 0.16 mmol). The reaction was

allowed to stir at room temperature for 2 h then treated with tris-amine (100 mg). The reaction was allowed to stand for 15 min at room temperature after which the resin was removed by filtration. The filtrate was concentrated under vacuum to afford the crude product. The crude residue was purified by flash chromatography (silica gel, 50% EtOAc/Hex) to afford the desired product as an off white powder (74 mg, 92 % yield). ^{1}H-NMR ($CDCl_3$): δ 8.15(d, 1H), 7.55 (s, 1H), 7.39 (m, 4H), 7.25 (d, 1H), 7.16 (m, 2H), 7.09 (m, 1H), 6.70 (m, 2H), 4.90 (q, 1H), 4.83 (s, 3H), 3.11 (s, 3H), 1.22 (d, 3H), 1.09 (s, 9H); MS (ESI) 506 (MH^+).

EXAMPLE 8

Preparation of 4-tert-Butyl-N-{1-[3-(4-methoxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzamide

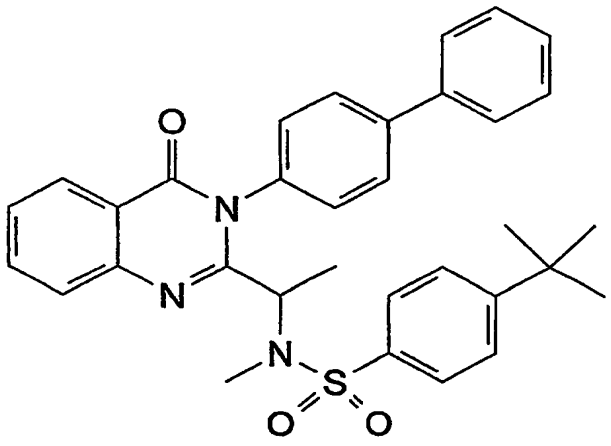


To a suspension of the 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one (50 mg, 0.16 mmol) stirring in 2 mL DCM was added TEA (19 mg, 0.19 mmol) followed by the addition of neat 4-tert-butyl-benzoyl chloride (31 mg, 0.16 mmol). The reaction was allowed to stir at room temperature for 2 h then treated with tris-amine (100 mg). The reaction was allowed to stand for 15 min at room temperature after which the resin was removed by filtration. The filtrate was concentrated under vacuum to afford the crude product. The crude residue was purified by flash chromatography (silica gel, 50% EtOAc/Hex) to afford

the desired product as an off white powder (73 mg, 97 % yield). ^{1}H-NMR ($CDCl_3$): δ 8.15 (d, 1H), 7.55 (m, 1H), 7.39 (m, 4H), 7.25 (d, 1H), 7.16 (m, 2H), 7.09 (m, 1H), 6.70 (m, 2H), 4.90 (q, 1H), 4.83 (s, 3H), 3.11 (s, 3H) 1.22 (d, 3H), 1.09 (s, 9H); MS (ESI) 470 (MH^+) .

EXAMPLE 9

Preparation of N-[1-(3-Biphenyl-4-yl-4-oxo-3,4-dihydro-quinazolin-2-yl)-ethyl]-4-tert-butyl-N-methyl-benzenesulfonamide

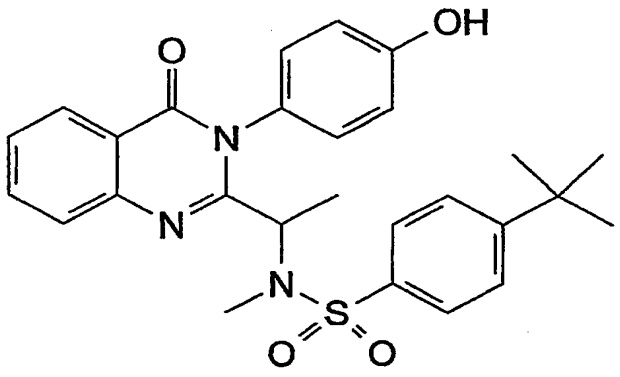


An oven-dried flask charged with N-{1-[3-(4-bromo-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-4-tert-butyl-N-methyl-benzenesulfonamide (103 mg, 0.19 mmol) was diluted with 2 mL of a nitrogen-purged solution of DME/H_2O (1:1). The resulting reaction mixture was then treated with K_2CO_3 (78.8 mg, 0.57 mmol) and phenyl boronic acid (46.3 mg, 0.38 mmol) at rt under a nitrogen atmosphere. In a separate oven dried vial containing triphenyl phosphine (43.9 mg, 0.17 mmol) and Pd_2dba_3:$CHCl_3$ (17 mg, 0.019 mmol) was placed 1 mL of the nitrogen purged DME/H_2O solution (1:1). The contents of the vial were stirred until the Pd(0) was completely dissolved. The premixed palladium solution was then added to the reaction mixture and heated to 70 °C under nitrogen for 16 h. The reaction mixture was cooled to rt and concentrated under vacuum. The resulting residue was then taken up in EtOAc and filtered through a plug of silica. The filtrate was concentrated

under vacuum to afford a crude residue that was purified by chromatography (silica gel, 0-75% EtOAC:Hex) to afford the desired product as a white solid (74 mg, 71% yield). ^{1}H-NMR ($CDCl_3$): δ 8.26 (d, 1H), 7.88 (d, 1H), 7.76 (d, 1H), 7.67 (m, 4H), 7.45 (m, 7H), 7.23 (m, 3H), 4.99 (q, 1H), 3.20 (s, 3H), 1.33 (d, 3H), 1.16 (s, 9H); MS (ESI) 552 (MH^+).

EXAMPLE 10

Preparation of 4-tert-Butyl-N-{1-[3-(4-hydroxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide

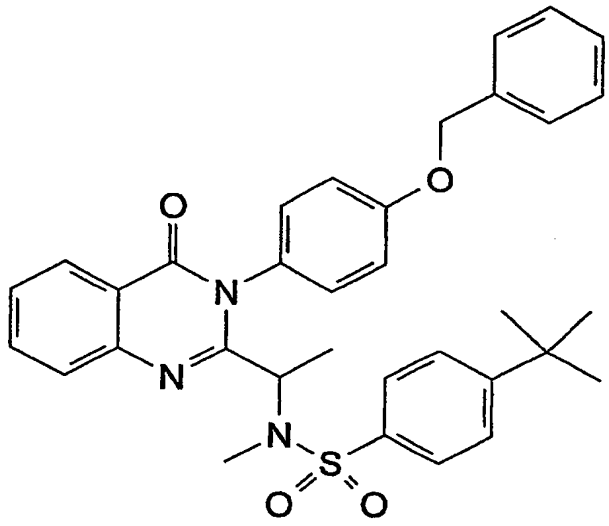


To a suspension of the 4-tert-butyl-N-{1-[3-(4-methoxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide (0.5 g, 1.07 mmol) stirring in 15 mL DCM was added boron tribromide (5 mL, 5 mmol 1M in DCM). The reaction was allowed to stir at room temperature for 15 min after which TLC analysis indicated that starting material was completely consumed. The reaction was quenched with 20 mL brine and the resulting mixture was transferred to a separatory funnel. The layers were separated and the aqueous layer extracted with $CHCl_3$ (2 x 25 mL). The combined organics were washed with brine, dried over $MgSO_4$, and concentrated under vacuum to afford a crude residue that was purified by chromatography (silica gel, 0-75% EtOAc:Hex), yielding the desired product as a white solid (0.735 g, 95 %). ^{1}H-NMR ($CDCl_3$): δ 8.26 (d, 1H), 7.67 (t, 1H), 7.51 (d, 2H), 7.45 (t, 1H), 7.36 (m, 2H), 7.26

(d, 2H), 6.98 (m, 1H), 6.90 (m, 2H), 5.00 (q, 1H), 3.19 (s, 3H), 1.28 (d, 3H), 1.17 (s, 9H); MS (ESI) 492 (MH^+).

EXAMPLE 11

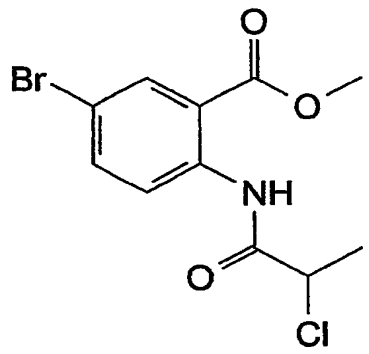
Preparation of N-{1-[3-(4-Benzyloxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-4-tert-butyl-N-methyl-benzenesulfonamide



To a solution of 4-tert-butyl-N-{1-[3-(4-hydroxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide (50 mg, 0.11 mmol) in anhydrous THF (2 mL) were added triphenylphosphine (0.115 mg, 0.44 mmol), diisopropyl azodicarboxylate (88.9 mg, 0.44 mmol), and benzyl alcohol (48.5 mg, 0.44 mmol) at 0 °C. The mixture was stirred for 1 h at this temperature and then allowed to warm to room temperature and stirred overnight. The solvent was evaporated under reduced pressure, and the crude residue was purified by chromatography (silica gel, 0-50% EtOAc:Hex) to yield the desired product as a white solid (48 mg, 80 %). ^{1}H-NMR ($CDCl_3$): δ 8.22 (d, 1H), 7.64 (m, 1H), 7.49 (m, 5H), 7.42 (m, 3H), 7.34 (m, 2H), 7.24 (m, 3H), 7.10 (m, 2H), 5.15 (s, 2H), 4.99 (q, 1H), 3.19 (s, 3H), 1.30 (d, 3H), 1.16 (s, 9H); MS (ESI) 582 (MH^+).

EXAMPLE 12

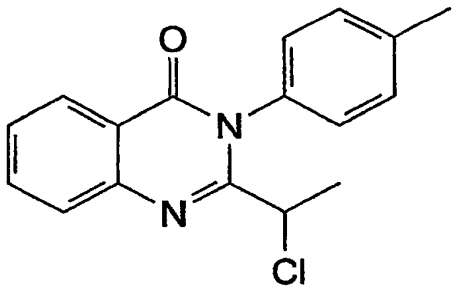
Preparation of 5-Bromo-2-(2-chloro-propionylamino)-benzoic acid methyl ester



The title compound was prepared in a manner similar to that described in example 1 by replacing methyl anthranilate with 2-amino-5-bromo-benzoic acid methyl ester. ^{1}H-NMR ($CDCl_3$): δ 11.77 (broad, 1H), 8.64 (d, 1H), 8.18 (d, 1H), 7.65 (dd, 1H), 4.53 (q, 1H), 3.97 (s, 3H), 1.82 (d, 3H); MS (ESI) 320 (MH^+).

EXAMPLE 13

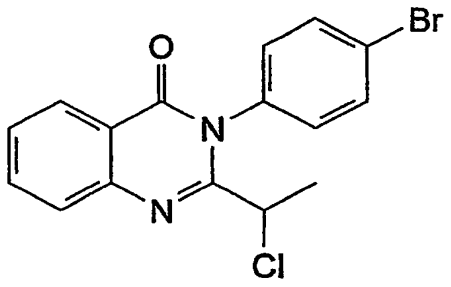
Preparation of 5-Bromo-2-(2-chloro-propionylamino)-benzoic acid methyl ester



The title compound was prepared in a manner similar to that described in example 3 by replacing *p*-anisidine with 4-methyl-phenylamine. ^{1}H-NMR ($CDCl_3$): δ 8.29 (d, 1H), 7.80 (d, 2H), 7.52 (m, 1H), 7.38 (s, 2H), 7.34 (d, 1H), 7.07 (m, 1H), 4.62 (q, 1H), 2.46 (s, 3H), 1.87 (d, 3H); MS (ESI) 299 (MH^+).

EXAMPLE 14

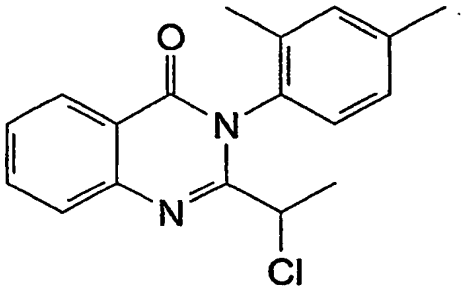
Preparation of 3-(4-Bromo-phenyl)-2-(1-chloro-ethyl)-3H-quinazolin-4-one



The title compound was prepared in a manner similar to that described in example 3 by replacing *p*-anisidine with 4-bromo-phenylamine. ^{1}H-NMR ($CDCl_3$): δ 8.28 (d, 1H), 7.81 (m, 2H), 7.70 (m, 2H), 7.54 (m, 1H), 7.39 (m, 1H), 7.08 (m, 1H), 4.55 (q, 1H), 1.88 (d, 3H); MS (ESI) 365 (MH^+).

EXAMPLE 15

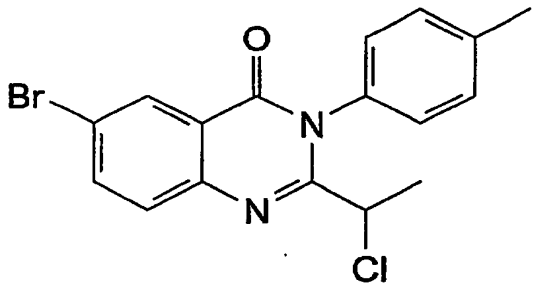
Preparation of 2-(1-Chloro-ethyl)-3-(2,4-dimethyl-phenyl)-3H-quinazolin-4-one



The title compound was prepared in a manner similar to that described in example 3 by replacing *p*-anisidine with 2,4-dimethyl-phenylamine. ^{1}H-NMR ($CDCl_3$): δ 8.33 (d, 1H), 7.83 (m, 2H), 7.54 (m, 1H), 7.26 (m, 2H), 6.95 (d, 1H), 4.73 (q, 1H), 2.44 (s, 3H), 2.22 (s, 1.5H), 2.06 (s, 1.5H), 1.89 (m, 1H); MS (ESI) 313 (MH^+).

EXAMPLE 16

Preparation of 6-Bromo-2-(1-chloro-ethyl)-3-p-tolyl-3H-quinolin-4-one

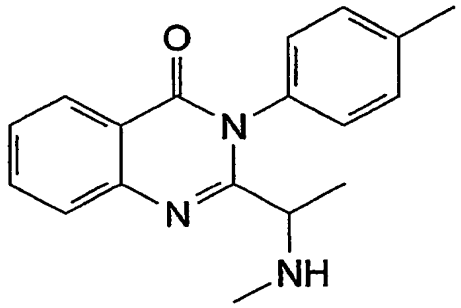


The title compound was prepared in a manner similar to that described in example 3 by replacing 2-(2-chloro-propionylamino)-benzoic acid with 5-bromo-2-(2-chloro-propionylamino)-benzoic acid and *p*-

anisidine with 4-methyl-phenylamine. ^{1}H-NMR ($CDCl_3$): δ 8.40 (m, 1H), 7.87 (m, 1H), 7.67 (d, 1H), 7.37 (m, 3H), 7.04 (m, 1H), 4.59 (q, 1H), 2.46 (s, 3H), 1.84 (d, 3H); MS (ESI) 377 (MH^+).

EXAMPLE 17

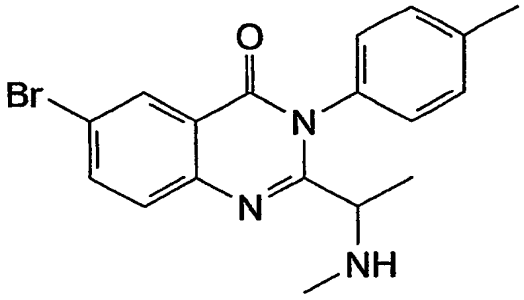
Preparation of 2-(1-Methylamino-ethyl)-3-p-tolyl-3H-quinazolin-4-one



The title compound was prepared in a manner similar to that described in example 5 by replacing 2-(1-chloro-ethyl)-3-(4-methoxy-phenyl)-3H-quinazolin-4-one with 2-(1-chloro-ethyl)-3-p-tolyl-3H-quinazolin-4-one. ^{1}H-NMR (CD_3OD): δ 8.28 (d, 1H), 7.77 (m, 1H), 7.71 (m, 1H), 7.47 (m, 1H), 7.36 (m, 2H), 7.12 (m, 2H), 3.37 (q, 1H), 2.46 (s, 3H), 2.28 (s, 3H), 1.24 (d, 3H); MS (ESI) 294 (MH^+).

EXAMPLE 18

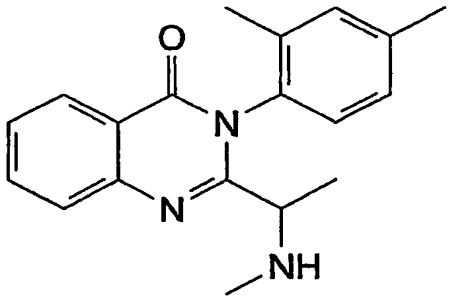
Preparation of 6-Bromo-2-(1-methylamino-ethyl)-3-p-tolyl-3H-quinazolin-4-one



The title compound was prepared in a manner similar to that described in example 5 by replacing 2-(1-chloro-ethyl)-3-p-tolyl-3H-quinazolin-4-one with 6-bromo-2-(1-chloro-ethyl)-3-p-tolyl-3H-quinazolin-4-one. ^{1}H-NMR (CD_3OD): δ 8.39 (d, 1H), 7.84 (m, 1H), 7.59 (d, 1H), 7.37 (m, 2H), 7.11 (m, 2H), 3.36 (q, 1H), 2.46 (s, 3H), 2.26 (s, 3H), 1.57 (broad, 1H), 1.23 (d, 3H); MS (ESI) 317 (MH^+).

EXAMPLE 19

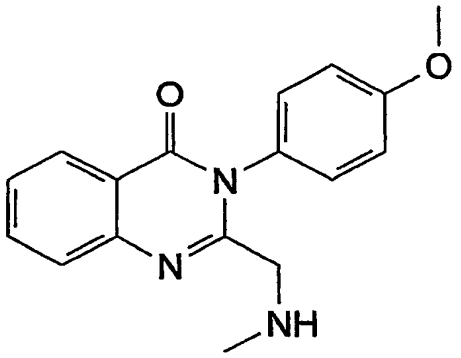
Preparation of 3-(2,4-Dimethyl-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one



The title compound was prepared in a manner similar to that described in example 5 by replacing 2-(1-chloro-ethyl)-3-(4-methoxy-phenyl)-3H-quinazolinon-4-one with 2-(1-chloro-ethyl)-3-(2,4-dimethyl-phenyl)-3H-quinazolin-4-one. ^{1}H-NMR (CD_3OD): δ 8.29 (d, 1H), 7.75 (m, 2H), 7.47 (t, 1H), 7.14 (s, 1H), 6.85 (d, 2H), 3.38 (q, 1H), 2.39 (s, 6H), 2.29 (s, 3H), 1.25 (d, 3H); MS (ESI) 308 (MH^+).

EXAMPLE 20

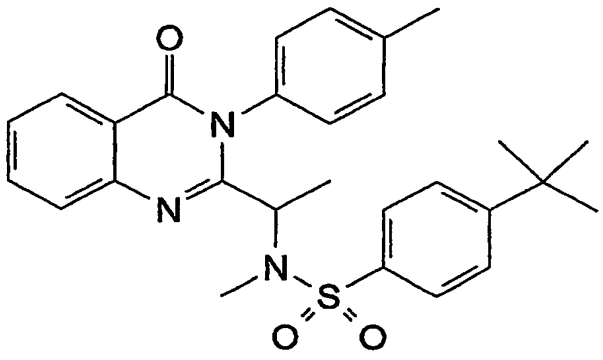
Preparation of 3-(4-Methoxy-phenyl)-2-methylaminomethyl-3H-quinazolin-4-one



The title compound was prepared in a manner similar to that described in example 5 by replacing 2-(1-chloro-ethyl)-3-(4-methoxy-phenyl)-3H-quinazolinon-4-one with 2-chloromethyl-3-(4-methoxy-phenyl)-3H-quinazolin-4-one. ^{1}H-NMR (CD_3OD): δ 8.27 (d, 1H), 7.93 (m, 1H), 7.86 (d, 1H), 7.65 (t, 1H), 7.43 (m, 1H), 7.33 (m, 1H), 7.19 (m, 2H), 4.08 (s, 2H), 3.92 (s, 3H), 2.74 (s, 3H); MS (ESI) 296 (MH^+).

EXAMPLE 21

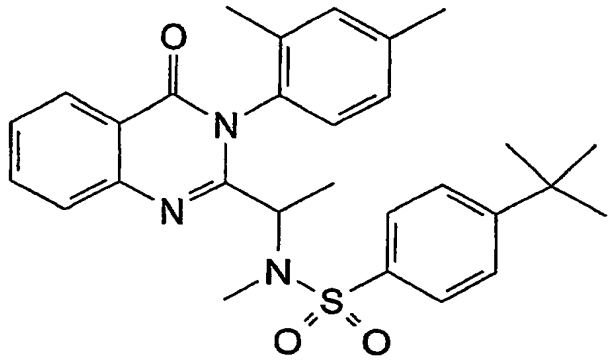
Preparation of 4-tert-Butyl-N-methyl-N-[1-(4-oxo-3-p-tolyl-3,4-dihydro-quinazolin-2-yl)-ethyl]-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 7 by replacing 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one with 2-(1-methylamino-ethyl)-3-p-tolyl-3H-quinazolin-4-one. ^{1}H-NMR ($CDCl_3$): δ 8.22 (m, 1H), 7.63 (m, 1H), 7.51 (m, 2H), 7.44 (m, 3H), 7.33 (m, 2H), 7.23 (m, 2H), 7.06 (m, 1H), 4.95 (q, 1H), 3.19 (s, 3H), 2.48 (s, 3H), 1.30 (d, 3H), 1.16 (s, 9H); MS (ESI) 490 (MH^+).

EXAMPLE 22

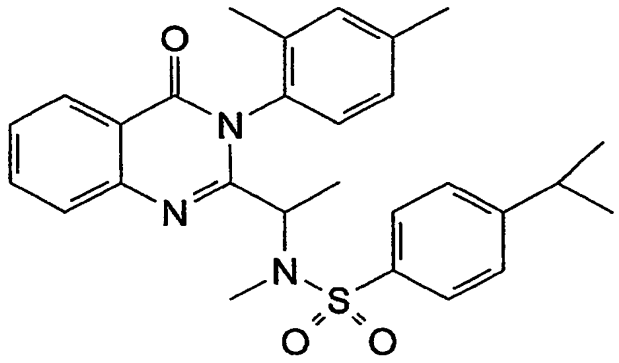
Preparation of 4-tert-Butyl-N-{1-[3-(2,4-dimethyl-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 7 by replacing 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one with 3-(2,4-dimethyl-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one. (mixture of rotomers) ^{1}H-NMR ($CDCl_3$): δ 8.30 (m, 1H), 7.72 (m, 1H), 7.56 (m, 4H), 7.38 (m, 2H), 7.30 (m, 2H), 7.21 (m, 1H), 5.03 (m, 1H), 3.15 (s, 1.5H), 3.01 (s, 1.5H), 2.47 (s, 1.5H), 2.45 (s, 1.5H), 2.26 (s, 1.5H), 2.04 (s, 1.5H), 1.31 (s, 4.5H), 1.24 (m, 3H), 1.21 (s, 4.5H); MS (ESI) 504 (MH^+).

EXAMPLE 23

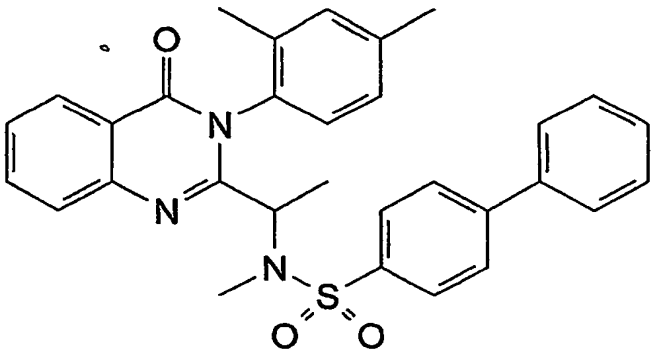
Preparation of N-{1-[3-(2,4-Dimethyl-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-4-isopropyl-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 22 by replacing 4-tert-butyl-benzenesulfonyl chloride with 4-isopropyl-benzenesulfonyl chloride. (mixture of rotomers) ^{1}H-NMR ($CDCl_3$): δ 8.26 (m, 1H), 7.71 (m, 1H), 7.51 (m, 4H), 7.34 (m, 2H), 7.18 (m, 3H), 5.0 (m, 1H), 3.11 (s, 1.5H), 2.97 (s, 1.5H), 2.85 (m, 1H), 2.44 (s, 1.5H), 2.42 (s, 1.5H), 2.19 (s, 1.5H), 2.01 (s, 1.5H), 1.21 (m, 6H), 1.12 (m, 3H); MS (ESI) 490 (MH^+).

EXAMPLE 24

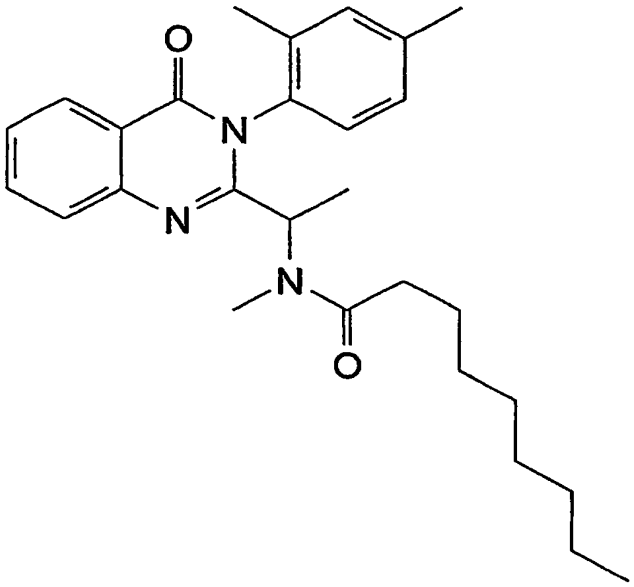
Preparation of Biphenyl-4-sulfonic acid {1-[3-(2,4-dimethyl-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-methy-l-amide



The title compound was prepared in a manner similar to that described in example 22 by replacing 4-tert-butyl-benzenesulfonyl chloride with biphenyl-4-sulfonyl chloride. (mixture of rotomers) ^{1}H-NMR ($CDCl_3$): δ 8.27 (m, 1H), 7.68 (m, 3H), 7.56 (m, 6H), 7.31 (m, 1H), 7.19 (m, 1H), 6.98 (m, 1H), 5.04 (m, 1H), 3.17 (s, 1.5H), 3.03 (s, 1.5H), 2.45 (s, 1.5H), 2.44 (s, 1.5H), 2.22 (s, 1.5H), 2.02 (s, 1.5H), 1.24 (m, 3H); MS (ESI) 524 (MH^+).

EXAMPLE 25

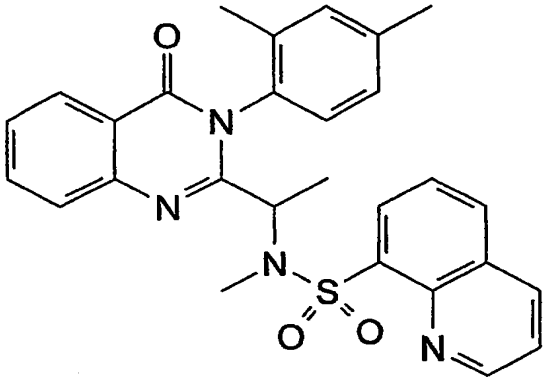
Preparation of Nonanoic acid {1-[3-(2,4-dimethyl-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-methyl-amide



The title compound was prepared in a manner similar to that described in example 8 by replacing 4-tert-butyl-benzoyl chloride with octanoyl chloride and 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one with 3-(2,4-dimethyl-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one. (mixture of rotomers) ^{1}H-NMR ($CDCl_3$): δ 8.32 (m, 1H), 7.80 (m, 2H), 7.55 (m, 1H), 7.19 (m, 2H), 7.06 (m, 1H), 5.44 (q, 1H), 2.92 (m, 3H), 2.39 (m, 3H), 2.25 (m, 2H), 2.03 (m, 3H), 1.47 (m, 5H), 1.29 (m, 10H), 0.9 (m, 3H); MS (ESI) 448 (MH^+).

EXAMPLE 26

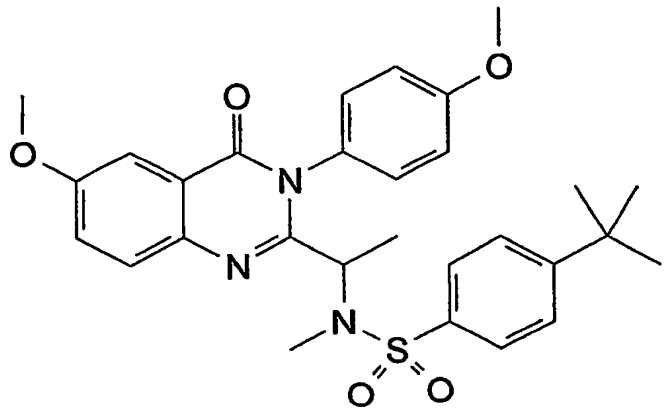
Preparation of Quinoline-8-sulfonic acid {1-[3-(2,4-dimethyl-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-methyl-amide



The title compound was prepared in a manner similar to that described in example 22 by replacing 4-tert-butyl-benzenesulfonyl chloride with quinoline-8-sulfonyl chloride. (mixture of rotomers) ^{1}H-NMR ($CDCl_3$): δ 8.56 (m, 1H), 8.49 (m, 0.5H), 8.34 (m, 1H), 8.19 (m, 1H), 7.97 (m, 1H), 7.89 (m, 0.5H), 7.77 (m, 1H), 7.54 (m, 3H), 7.40 (m, 1H), 7.31 (m, 1H), 7.22 (m, 1H), 7.10 (m, 1H), 5.66 (m, 1H), 3.32 (s, 3H), 2.48 (m, 3H), 2.10 (m, 3H), 1.18 (m, 3H); MS (ESI) 499 (MH^+).

EXAMPLE 27

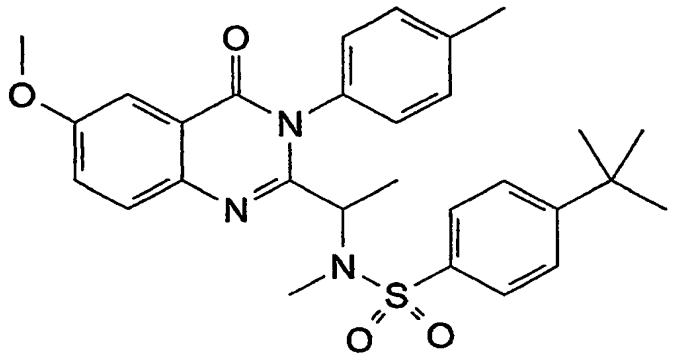
Preparation of 4-tert-Butyl-N-{1-[6-methoxy-3-(4-methoxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 7 by replacing 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one with 6-methoxy-3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one. ^{1}H-NMR ($CDCl_3$): δ 7.58 (d, 1H), 7.50 (d, 2H), 7.47 (m, 1H), 7.24 (m, 4H), 7.17 (m, 1H), 7.06 (m, 2H), 4.96 (q, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 3.15 (s, 3H), 1.28 (d, 3H), 1.18 (s, 9H); MS (ESI) 536 (MH^+).

EXAMPLE 28

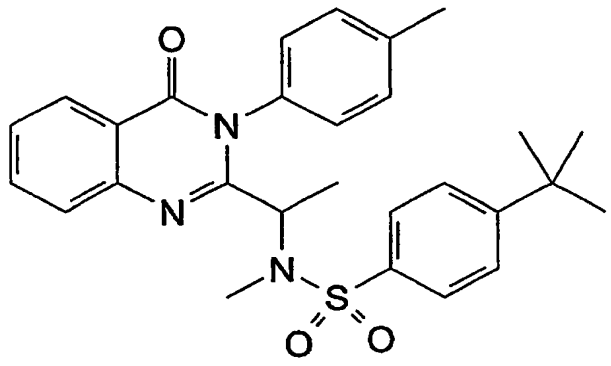
Preparation of 4-tert-Butyl-N-[1-(6-methoxy-4-oxo-3-p-tolyl-3,4-dihydro-quinazolin-2-yl)-ethyl]-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 7 by replacing 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one with 6-methoxy-2-(1-methylamino-ethyl)-3-p-tolyl-3H-quinazolin-4-one. ^{1}H-NMR ($CDCl_3$): δ 7.58 (d, 1H), 7.50 (d, 2H), 7.44 (m, 1H), 7.34 (m, 1H), 7.24 (m, 5H), 7.05 (m, 1H), 4.93 (q, 1H), 3.88 (s, 3H), 3.15 (s, 3H), 2.48 (s, 3H), 1.28 (d, 3H), 1.18 (s, 9H); MS (ESI) 520 (MH^+).

EXAMPLE 29

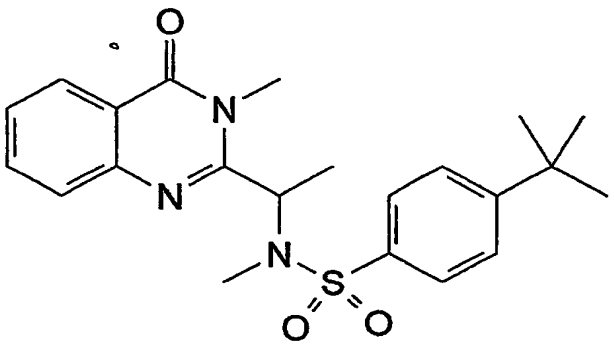
Preparation of 4-tert-Butyl-N-methyl-N-[1-(4-oxo-3-p-tolyl-3,4-dihydro-quinazolin-2-yl)-ethyl]-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 7 by replacing 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one with 2-(1-methylamino-ethyl)-3-p-tolyl-3H-quinazolin-4-one. ^{1}H-NMR ($CDCl_3$): δ 8.22 (m, 1H), 7.63 (m, 1H), 7.51 (m, 2H), 7.44 (m, 3H), 7.33 (t, 2H), 7.22 (m, 2H), 7.06 (m, 1H), 4.95 (q, 1H), 3.19 (s, 3H), 2.48 (s, 3H), 1.30 (d, 3H), 1.16 (s, 9H); MS (ESI) 490 (MH^+).

EXAMPLE 30

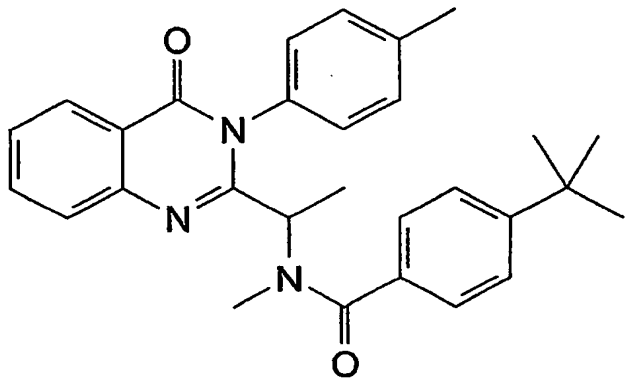
Preparation of 4-tert-Butyl-N-methyl-N-[1-(3-methyl-4-oxo-3,4-dihydro-quinazolin-2-yl)-ethyl]-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 7 by replacing 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one with 3-methyl-2-(1-methylamino-ethyl)-3H-quinazolin-4-one. ^{1}H-NMR ($CDCl_3$): δ 8.25 (m, 1H), 7.76 (d, 2H), 7.52 (m, 1H), 7.45 (m, 3H), 5.53 (q, 1H), 3.84 (s, 3H), 2.81 (s, 3H), 1.41 (d, 3H), 1.27 (s, 9H); MS (ESI) 414 (MH^+).

EXAMPLE 31

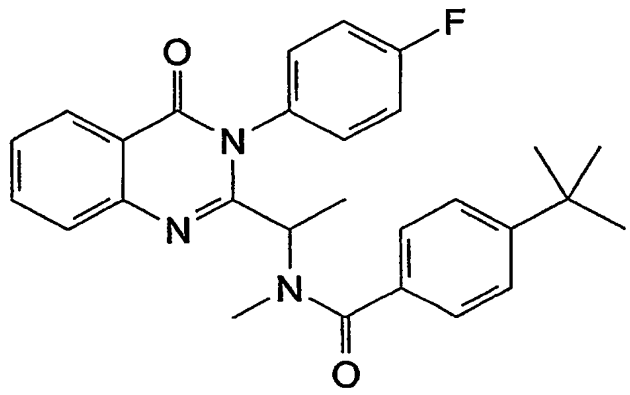
Preparation of 4-tert-Butyl-N-methyl-N-[1-(4-oxo-3-p-tolyl-3,4-dihydro-quinazolin-2-yl)-ethyl]-benzamide



The title compound was prepared in a manner similar to that described in example 8 by replacing 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one with 2-(1-methylamino-ethyl)-3-p-tolyl-3H-quinazolin-4-one. ^{1}H-NMR ($CDCl_3$): δ 8.28 (m, 1H), 7.76 (t, 1H), 7.69 (d, 1H), 7.48 (m, 2H), 7.36 (m, 4H), 7.28 (m, 1H), 7.19 (m, 1H), 6.96 (m, 1H), 5.43 (q, 1H), 3.10 (s, 3H), 2.41 (s, 3H), 1.49 (d, 3H), 1.31 (s, 9H); MS (ESI) 454 (MH^+).

EXAMPLE 32

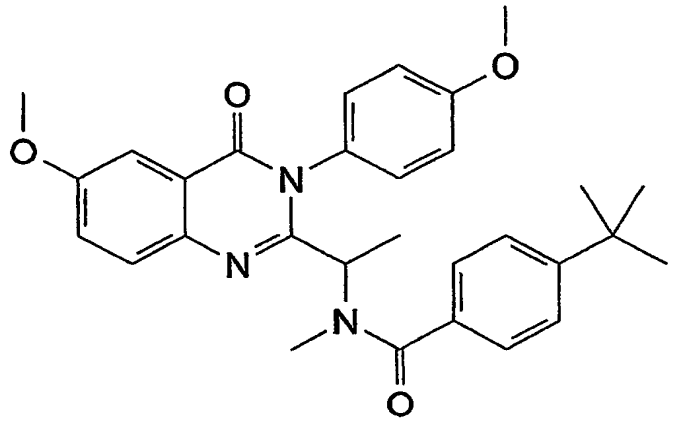
Preparation of 4-tert-Butyl-N-{1-[3-(4-fluoro-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzamide



The title compound was prepared in a manner similar to that described in example 8 by replacing 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one with 3-(4-fluoro-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one. ^{1}H-NMR ($CDCl_3$): δ 8.31 (d, 1H), 7.80 (t, 1H), 7.73 (m, 1H), 7.64 (m, 1H), 7.52 (t, 1H), 7.42 (m, 2H), 7.29 (m, 5H), 5.8 (q, 1H), 3.15 (s, 3H), 1.53 (d, 3H), 1.34 (s, 9H); MS (ESI) 458 (MH^+).

EXAMPLE 33

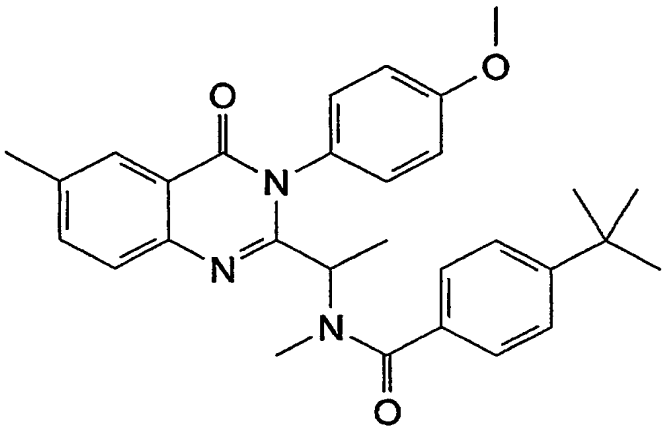
Preparation of 4-tert-Butyl-N-{1-[6-methoxy-3-(4-methoxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzamide



The title compound was prepared in a manner similar to that described in example 8 by replacing 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one with 6-methoxy-3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one. ^{1}H-NMR ($CDCl_3$): δ 7.63 (m, 2H), 7.48 (m, 1H), 7.37 (m, 3H), 7.28 (m, 2H), 7.21 (m, 1H), 7.04 (m, 2H), 5.46 (q, 1H), 3.91 (s, 3H), 3.83 (s, 3H), 1.48 (d, 3H), 1.31 (s, 9H); MS (ESI) 500 (MH^+).

EXAMPLE 34

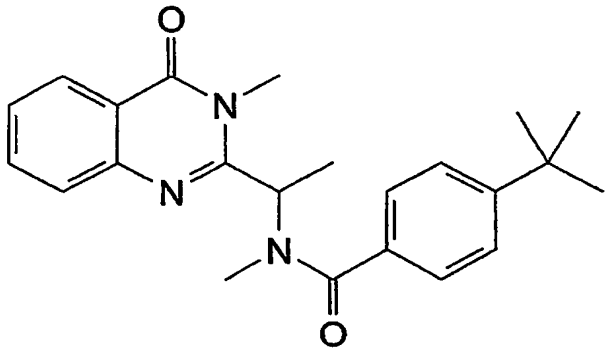
Preparation of 4-tert-Butyl-N-{1-[3-(4-methoxy-phenyl)-6-methyl-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzamide



The title compound was prepared in a manner similar to that described in example 8 by replacing 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one with 3-(4-methoxy-phenyl)-6-methyl-2-(1-methylamino-ethyl)-3H-quinazolin-4-one. ^{1}H-NMR ($CDCl_3$): δ 8.06 (m, 1H), 7.59 (m, 2H), 7.49 (m, 1H), 7.38 (m, 2H), 7.28 (m, 2H), 7.21 (m, 1H), 7.04 (m, 2H), 5.45 (q, 1H), 3.83 (s, 3H), 3.08 (s, 3H), 2.49 (s, 3H), 1.48 (d, 3H), 1.31 (s, 9H); MS (ESI) 484 (MH^+).

EXAMPLE 35

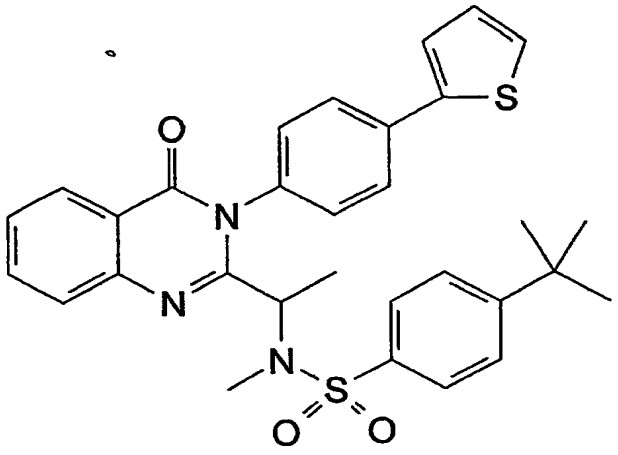
Preparation of 4-tert-Butyl-N-methyl-N-[1-(3-methyl-4-oxo-3,4-dihydro-quinazolin-2-yl)-ethyl]-benzamide



The title compound was prepared in a manner similar to that described in example 8 by replacing 3-(4-methoxy-phenyl)-2-(1-methylamino-ethyl)-3H-quinazolin-4-one with 3-methyl-2-(1-methylamino-ethyl)-3H-quinazolin-4-one. ^{1}H-NMR ($CDCl_3$): δ 8.65 (d, 1H), 7.59 (broad, 1H), 7.44 (m, 5H), 7.08 (t, 1H), 6.22 (q, 1H), 3.02 (s, 3H), 3.01 (s, 3H), 1.54 (d, 3H), 1.33 (s, 9H); MS (ESI) 378 (MH^+).

EXAMPLE 36

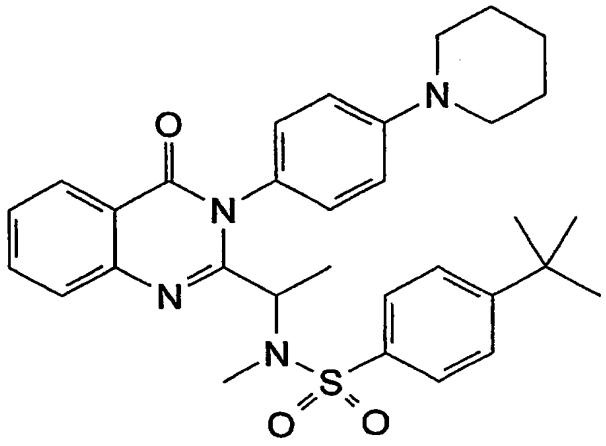
Preparation of 4-tert-Butyl-N-methyl-N-{1-[4-oxo-3-(4-thiophen-2-yl-phenyl)-3,4-dihydro-quinazolin-2-yl]-ethyl}-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 9 by replacing phenyl boronic acid with thiophene-2-boronic acid. ^{1}H-NMR ($CDCl_3$): δ 8.23 (m, 1H), 7.79 (m, 1H), 7.67 (m, 3H), 7.47 (m, 7H), 7.39 (m, 2H), 7.08 (m, 1H), 4.90 (q, 1H), 3.12 (s, 3H), 3.12 (s, 3H), 1.29 (d, 3H), 1.20 (s, 9H); MS (ESI) 558 (MH^+).

EXAMPLE 37

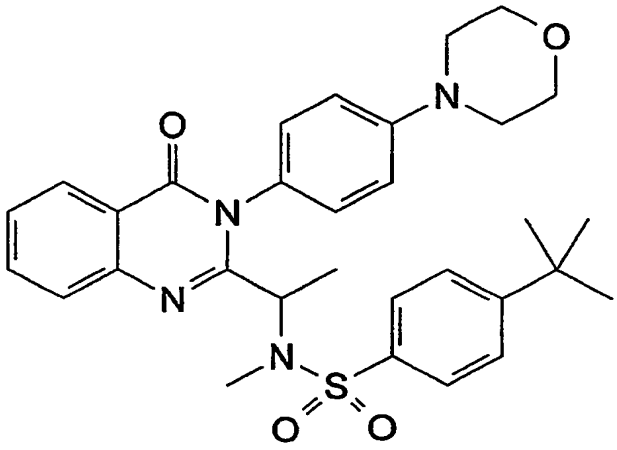
Preparation of 4-tert-Butyl-N-methyl-N-{1-[4-oxo-3-(4-piperidin-1-yl-phenyl)-3,4-dihydro-quinazolin-2-yl]-ethyl}-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 9 by replacing phenyl boronic acid with piperidine. ^{1}H-NMR ($CDCl_3$): δ 8.21 (m, 1H), 7.60 (m, 2H), 7.51 (d, 2H), 7.39 (m, 2H), 7.20 (m, 2H), 7.13 (m, 1H), 7.00 (m, 2H), 5.01 (q, 1H), 3.29 (m, 4H), 3.23 (s, 3H), 1.74 (m, 4H), 1.30 (d, 3H), 1.26 (m, 2H), 1.14 (s, 9H);MS (ESI) 559 (MH^+).

EXAMPLE 38

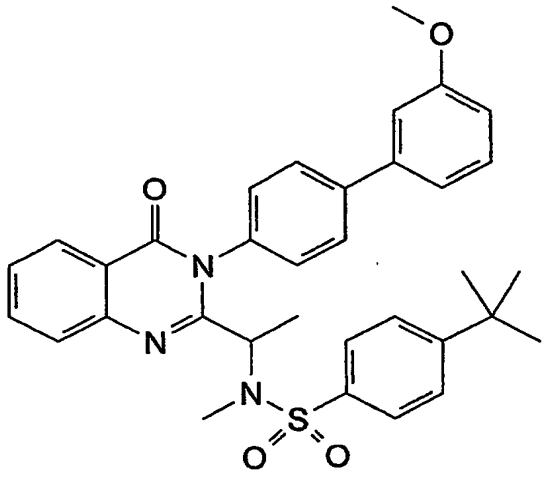
Preparation of 4-tert-Butyl-N-methyl-N-{1-[3-(4-morpholin-4-yl-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 9 by replacing phenyl boronic acid with morpholine. ^{1}H-NMR ($CDCl_3$): δ 8.22 (d, 1H), 7.62 (m, 1H), 7.52 (d, 2H), 7.424 (m, 2H), 7.30 (d, 1H), t.22 (d, 2H), 7.14 (d, 1H), 7.03 (m, 2H), 5.01 (q, 1H), 3.90 (s, 3H), 3.28 (m, 3H), 3.21 (s, 3H), 1.31 (d, 3H), 1.14 (s, 9H); MS (ESI) 561 (MH^+).

EXAMPLE 39

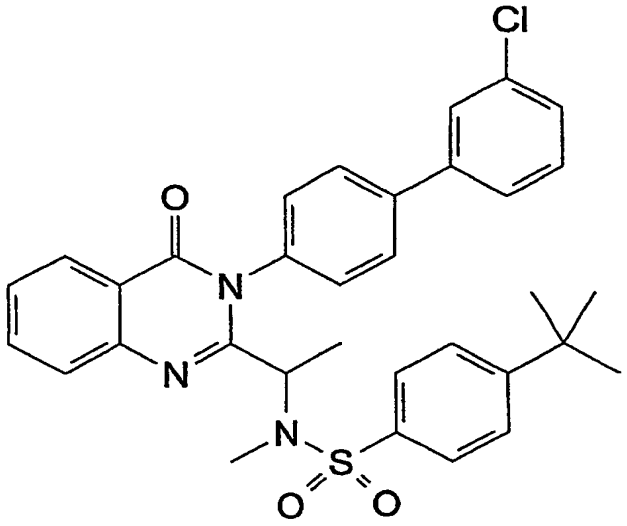
Preparation of 4-tert-Butyl-N-{1-[3-(3'-methoxy-biphenyl-4-yl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 9 by replacing phenyl boronic acid with 3-methoxy-phenyl boronic acid. ^{1}H-NMR ($CDCl_3$): δ 8.25 (d, 1H), 7.87 (m, 1H), 7.75 (m, 1H), 7.65 (m, 2h), 7.52 (m, 2H), 7.41 (m, 3H), 7.25 (m, 5H), 6.95 (m, 1H), 4.98 (q, 1H), 3.89 (s, 3H), 3.20 (s, 3H), 1.31 (d, 3H), 1.16 (s, 9H); MS (ESI) 582 (MH^+).

EXAMPLE 40

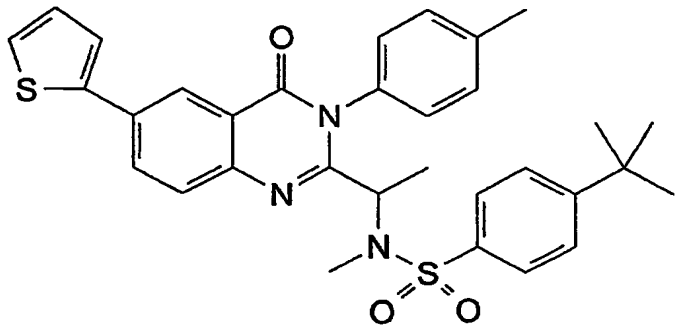
Preparation of 4-tert-Butyl-N-{1-[3-(3'-chloro-biphenyl-4-yl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 9 by replacing phenyl boronic acid with 3-chloro-phenyl boronic acid. ^{1}H-NMR ($CDCl_3$): δ 8.25 (d, 1H), 7.86 (m, 1H), 7.73 (m, 1H), 7.66 (m, 3H), 7.55 (m, 1H), 7.52 (d, 2H), 7.46 (t, 1H), 7.40 (m, 3H), 7.26 (m, 3H), 4.97 (q, 1H), 3.16 (d, 3H), 1.31 (d, 3H), 1.17 (s, 9H); MS (ESI) 587 (MH^+).

EXAMPLE 41

Preparation of 4-tert-Butyl-N-{1-[3-(4-methoxy-phenyl)-4-oxo-6-thiophen-2-yl-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide

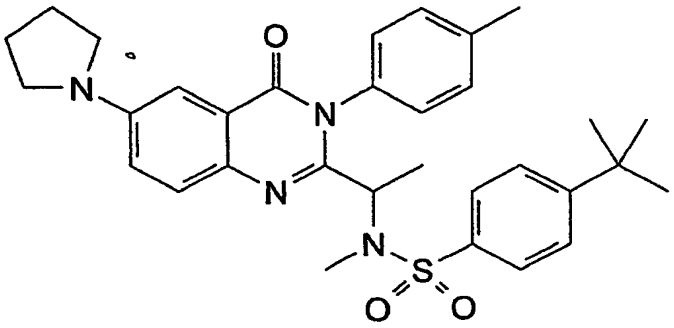


The title compound was prepared in a manner similar to that described in example 9 by replacing phenyl boronic acid with thiophene-2-boronic acid and N-{1-[3-(4-bromo-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-4-tert-butyl-N-methyl-benze

Nesulfonamide with N-[1-(6-bromo-4-oxo-3-p-tolyl-3,4-dihydro-quinazolin-2-yl)-ethyl]-4-tert-butyl-N-methyl-benzenesulfonamide. ^{1}H-NMR ($CDCl_3$): δ 8.34 (d, 1H), 7.71 (m, 2H), 7.5 (d, 2H), 7.46 (m, 3H), 7.35 (d, 1H), 7.22 (m, 4H) 7.05 (d, 1H), 4.92 (q, 1H), 3.17 (s, 3H), 2.48 (s, 3H), 1.29 (d, 3H), 1.19 (s, 9H); MS (ESI) 570 (MH^+).

EXAMPLE 42

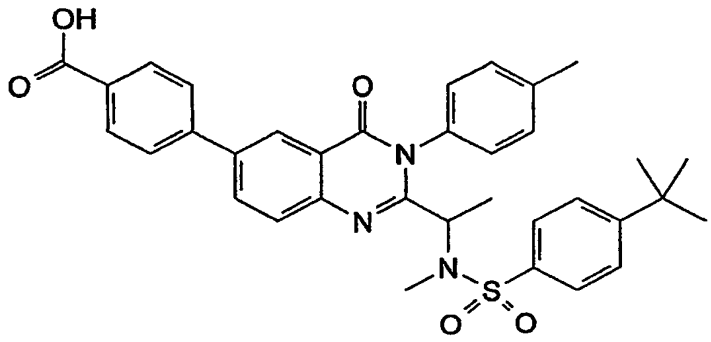
Preparation of 4-tert-Butyl-N-{1-[3-(4-methoxy-phenyl)-4-oxo-6-pyrrolidin-1-yl-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 41 by replacing thiophene-2-boronic acid with pyrrolidine. ^{1}H-NMR ($CDCl_3$): δ 7.51 (d, 2H), 7.43 (m, 2H), 7.33 (d, 1H), 7.24 (m, 3H), 7.17 (m, 1H), 7.05 (d, 1H), 6.93 (d, 1H), 4.92 (q, 1H), 3.35 (m, 4H), 3.12 (s, 3H), 2.47 (s, 3H), 2.04(m, 4H), 1.28 (d, 3H), 1.18 (s, 9H); MS (ESI) 559 (MH^+).

EXAMPLE 43

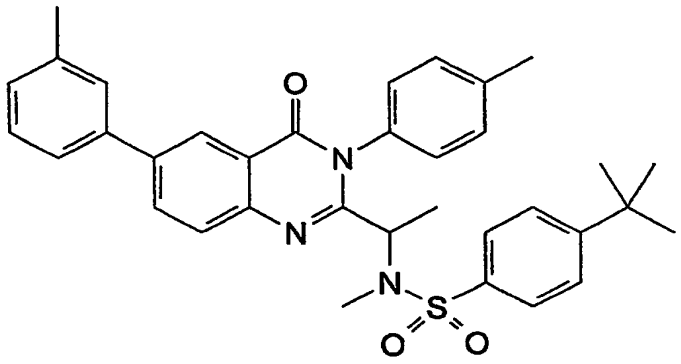
Preparation of 4-[2-{1-[(4-tert-Butyl-benzenesulfonyl)-methyl-amino]-ethyl}-3-(4-methoxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-6-yl]-benzoic acid



The title compound was prepared in a manner similar to that described in example 41 by replacing thiophene-2-boronic acid with 4-carboxy-phenyl boronic acid. ^{1}H-NMR ($CDCl_3$): δ 8.48 (d, 1H), 8.21 (m, 2H), 7.92 (m, 1H), 7.74 (d, 2H), 7.54 (d, 2H), 7.46 (m, 4H), 7.36 (m, 1H), 7.24 (m, 1H), 7.08 (m, 1H), 4.96 (q, 1H), 3.21 (s, 3H), 2.49 (s, 3H), 1.32 (d, 3H), 1.15 (s, 9H); MS (ESI) 610 (MH^+).

EXAMPLE 44

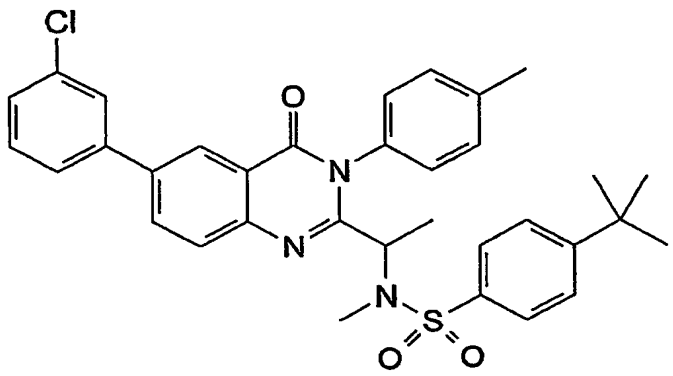
Preparation of 4-tert-Butyl-N-{1-[3-(4-methoxy-phenyl)-4-oxo-6-m-tolyl-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 41 by replacing thiophene-2-boronic acid with 3-methyl-phenyl boronic acid. ^{1}H-NMR ($CDCl_3$): δ 8.41 (m, 1H), 7.87 (m, 2H), 7.53 (m, 2H), 7.45 (m, 3H), 7.37 (m, 3H), 7.23 (m, 3H), 7.07 (m, 1H), 4.96 (q, 1H), 3.21 (s, 3H), 2.49 (s, 3H), 2.43 (s, 3H), 1.32 (d, 3H), 1.15 (s, 9H); MS (ESI) 580 (MH^+).

EXAMPLE 45

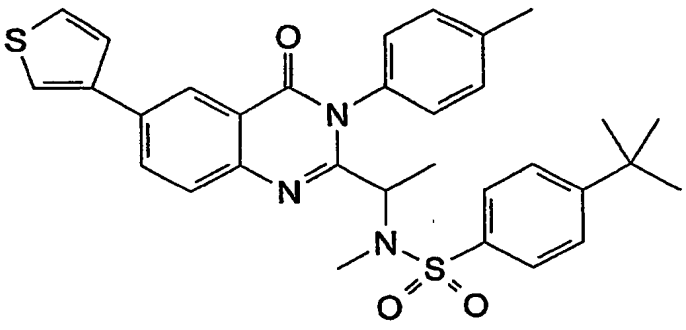
Preparation of 4-tert-Butyl-N-{1-[6-(3-chloro-phenyl)-3-(4-methoxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 41 by replacing thiophene-2-boronic acid with 3-chloro-phenyl boronic acid. ^{1}H-NMR ($CDCl_3$): δ 8.39 (d, 1H), 7.84 (m, 1H), 7.61 (m, 1H), 7.53 (m, 2H), 7.47 (m, 3H), 7.40 (d, 2H), 7.37 (m, 2H), 7.24 (m, 2H), 7.07 (m, 1H), 4.95 (q, 1H), 3.20 (s, 3H), 2.49 (s, 3H), 1.31 (d, 3H), 1.15 (s, 9H); MS (ESI) 601 (MH^+).

EXAMPLE 46

Preparation of 4-tert-Butyl-N-{1-[3-(4-methoxy-phenyl)-4-oxo-6-thiophen-3-yl-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide

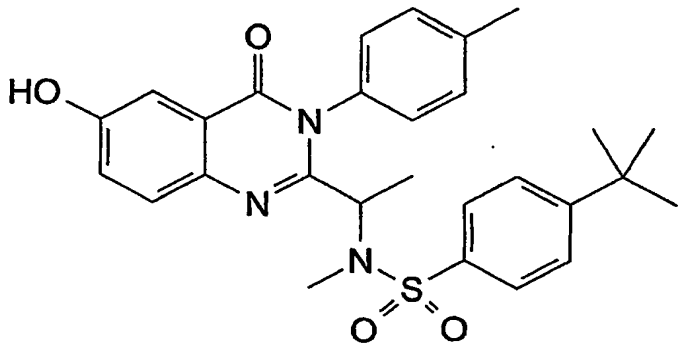


The title compound was prepared in a manner similar to that described in example 41 by replacing thiophene-2-boronic acid with 3-thiophene boronic acid. ^{1}H-NMR ($CDCl_3$): δ 8.33 (d, 1H), 7.71 (m, 1H),

7.50 (m, 3H), 7.44 (m, 3H), 7.35 (m, 1H), 7.22 (m, 4H), 7.04 (m, 1H), 4.91 (q, 1H), 3.17 (s, 3H), 2.48 (s, 3H), 1.29 (d, 3H), 1.17 (s, 9H); MS (ESI) 570 (MH^+).

EXAMPLE 47

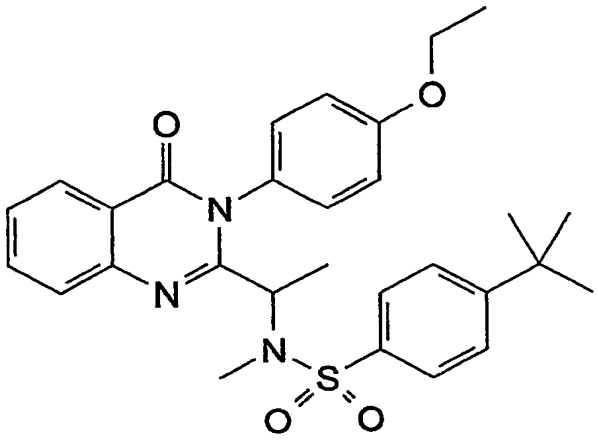
Preparation of 4-tert-Butyl-N-[1-(6-hydroxy-4-oxo-3-p-tolyl-3,4-dihydro-quinazolin-2-yl)-ethyl]-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 10 by replacing 4-tert-butyl-N-{1-[3-(4-methoxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide with 4-tert-butyl-N-[1-(6-methoxy-4-oxo-3-p-tolyl-3,4-dihydro-quinazolin-2-yl)-ethyl]-N-methyl-benzenesulfonamide. ^{1}H-NMR ($CDCl_3$): δ 7.82 (d, 1H), 7.49 (m, 3H), 7.42 (d, 1H), 7.36 (d, 1H), 7.24 (m, 4H), 7.06 (d, 1H), 6.21 (s, 1H), 4.94 (q, 1H), 3.13 (s, 3H), 2.48 (s, 3H), 1.27 (d, 3H), 1.18 (s, 9H); MS (ESI) 506 (MH^+).

EXAMPLE 48

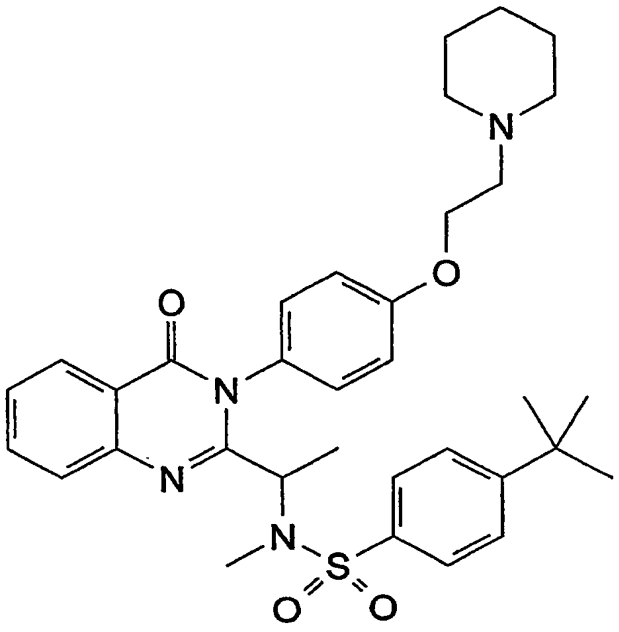
Preparation of 4-tert-Butyl-N-{1-[3-(4-ethoxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 11 by replacing benzyl alcohol with ethyl alcohol. ^{1}H-NMR ($CDCl_3$): δ 8.22 (d, 1H), 7.64 (t, 1H), 7.43 (m, 2H), 7.33 (d, 1H), 7.23 (m, 2H), 7.15 (d, 1H), 7.05 (dd, 2H), 4.98 (q, 1H), 4.13 (q, 2H), 3.19 (s, 3H), 1.47 (t, 3H), 1.29 (d, 3H), 1.16 (s, 9H); MS (ESI) 520 (MH^+).

EXAMPLE 49

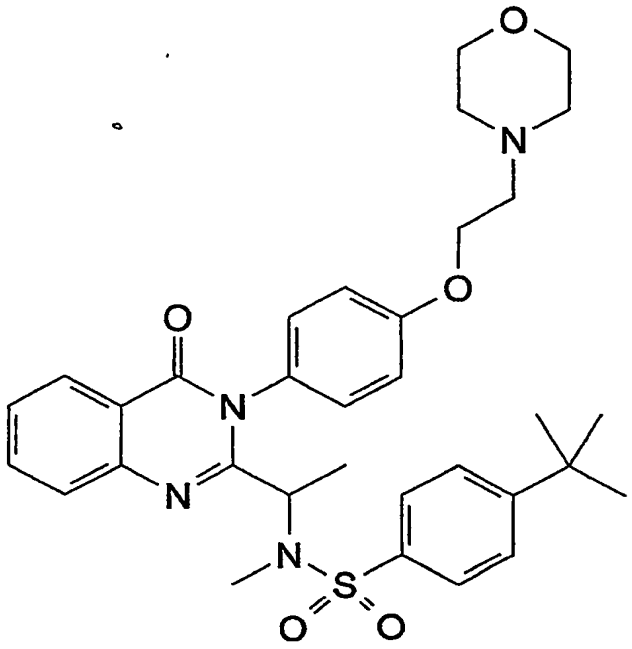
Preparation of 4-tert-Butyl-N-methyl-N-(1-{4-oxo-3-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-3,4-dihydro-quinazolin-2-yl}-ethyl)-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 11 by replacing benzyl alcohol with 2-piperidin-1-yl-ethanol. ^{1}H-NMR ($CDCl_3$): δ 8.23 (d, 1H), 7.67 (m, 2H), 7.46 (m, 4H), 7.30 (d, 2H), 7.15 (m, 2H), 7.06 (m, 1H), 5.00 (q, 1H), 4.50 (m, 2H), 3.76 (m, 2H), 3.54 (m, 2H), 3.07 (s, 3H), 1.28 (d, 3H), 1.17 (s, 9H); MS (ESI) 603 (MH^+).

EXAMPLE 50

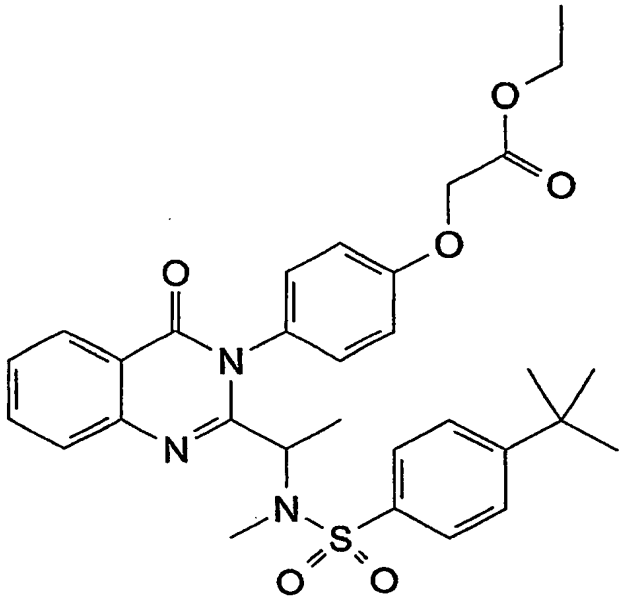
Preparation of 4-tert-Butyl-N-methyl-N-(1-{3-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-4-oxo-3,4-dihydro-quinazolin-2-yl}-ethyl)-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 11 by replacing benzyl alcohol with 2-morpholin-4-yl-ethanol. ^{1}H-NMR ($CDCl_3$): δ 8.25 (d, 1H), 7.69 (t, 1H), 7.53 (d, 2H), 7.46 (m, 3H), 7.31 (d, 2H), 7.15 (m, 2H), 7.07 (m, 1H), 5.00 (q, 1H), 4.52 (m, 2H), 4.01 (m, 4H) 3.71 (m, 2H), 3.58 (m, 2H), 3.09 (m, 2H), 3.03 (m, 2H), 2.72 (s, 3H), 1.28 (d, 3H), 1.21 (s, 9H); MS (ESI) 605 (MH^+).

EXAMPLE 51

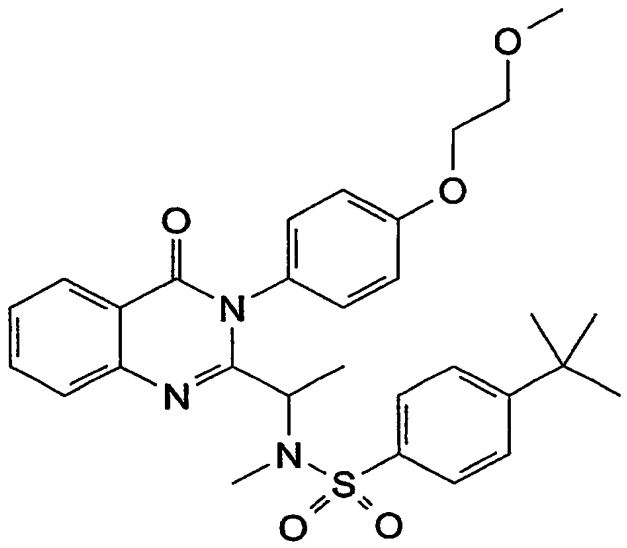
Preparation of [4-(2-{1-[(4-tert-Butyl-benzenesulfonyl)-methyl-amino]-ethyl}-4-oxo-4H-quinazolin-3-yl)-phenoxy]-acetic acid ethyl ester



The title compound was prepared in a manner similar to that described in example 11 by replacing benzyl alcohol with hydroxy-acetic acid ethyl ester. ^{1}H-NMR ($CDCl_3$): δ 8.22 (d, 1H, 7.65 (t, 1H), 7.50 (d, 3H), 7.44 (t, 1H), 7.36 (d, 1H), 7.27 (s, 2H), 7.16 (d, 1H), 7.10 (s, 2H), 4.94 (q, 1H), 4.71 (s, 2H), 4.31 (q, 2H), 3.17 (s, 3H), 1.33 (t, 3H), 1.26 (d, 2H), 1.18 (s, 9H); MS (ESI) 578 (MH^+).

EXAMPLE 52

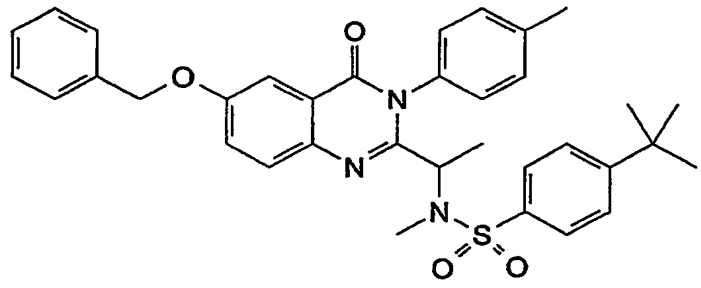
Preparation of 4-tert-Butyl-N-(1-{3-[4-(2-methoxy-ethoxy)-phenyl]-4-oxo-3,4-dihydro-quinazolin-2-yl}-ethyl)-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 11 by replacing benzyl alcohol with 2-methoxy-ethanol. ^{1}H-NMR ($CDCl_3$): δ 8.22 (d, 1H), 7.64 (t, 1H), 7.45 (m, 4H), 7.33 (d, 1h), 7.21 (m, 3H), 7.09 (s, 2H), 4.97 (q, 1H), 4.22 (t, 2H), 3.81 (t, 2H), 3.49 (s, 3H), 3.19 (d, 3H), 1.28 (d, 3H), 1.17 (s, 9H); MS (ESI) 550 (MH^+).

EXAMPLE 53

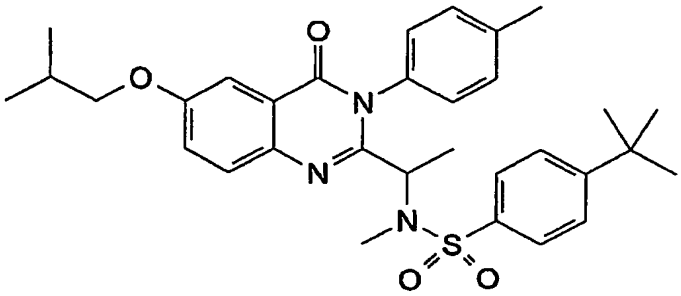
Preparation of N-[1-(6-Benzyloxy-4-oxo-3-p-tolyl-3,4-dihydro-quinazolin-2-yl)-ethyl]-4-tert-butyl-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 11 by replacing 4-tert-butyl-N-{1-[3-(4-hydroxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide with 4-tert-butyl-N-[1-(6-hydroxy-4-oxo-3-p-tolyl-3,4-dihydro-quinazolin-2-yl)-ethyl]-N-methyl-benzenesulfonamide. ^{1}H-NMR ($CDCl_3$): δ 7.67 (d, 1H), 7.50 (m, 2H), 7.44 (m, 4H), 7.39 (m, 2H), 7.34 (m, 2H), 7.30 (m, 2H), 7.24 (m, 1H), 7.05 (m, 1H), 5.13 (s, 2H), 4.93 (q, 1H), 3.14 (s, 3H), 2.48 (s, 3H), 1.28 (d, 3H), 1.18 (s, 9H); MS (ESI) 596 (MH^+).

EXAMPLE 54

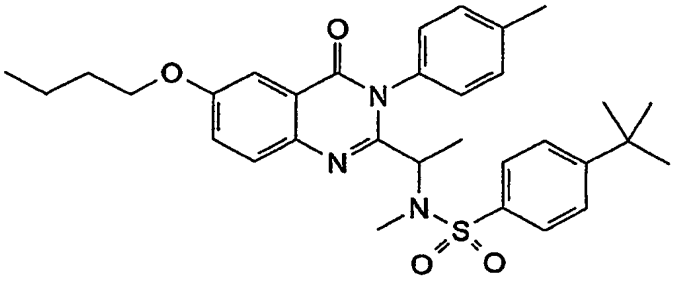
Preparation of 4-tert-Butyl-N-[1-(6-isobutoxy-4-oxo-3-p-tolyl-3,4-dihydro-quinazolin-2-yl)-ethyl]-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 53 by replacing benzyl alcohol with iso-butyl alcohol. ^{1}H-NMR ($CDCl_3$): δ 7.54 (d, 1H), 7.50 (m, 2H), 7.45 (m, 1H), 7.43 (m, 1H), 7.33 (m, 1H), 7.24 (m, 4H), 7.04 (m, 1H), 4.93 (q, 1H), 3.79 (d, 2H), 3.15 (s, 3H), 2.48 (s, 3H), 1.28 (d, 3H), 1.17 (s, 9H); MS (ESI) 562 (MH^+).

EXAMPLE 55

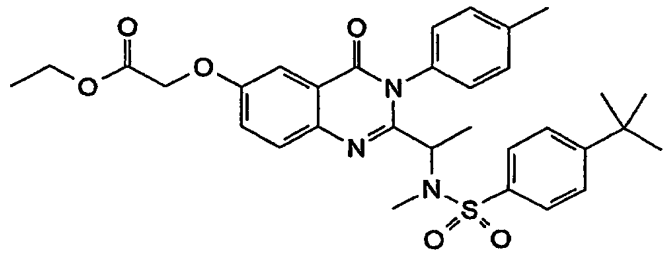
Preparation of N-[1-(6-Butoxy-4-oxo-3-p-tolyl-3,4-dihydro-quinazolin-2-yl)-ethyl]-4-tert-butyl-N-methyl-benzenesulfonamide



The title compound was prepared in a manner similar to that described in example 53 by replacing benzyl alcohol with n-butyl alcohol. ^{1}H-NMR ($CDCl_3$): δ 7.5 (m, 3H), 7.46 (m, 1H), 7.40 (m, 1H), 7.34 (m, 3H), 7.26 (m, 2H), 7.05 (m, 1H), 4.94 (q, 1H), 4.69 (s, 2H), 4.27 (q, 2H), 3.13 (s, 3H), 2.48 (s, 3H), 1.31 (t, 3H), 1.27 (d, 3H), 1.19 (s, 9H); MS (ESI) 562 (MH^+).

EXAMPLE 56

Preparation of (2-{1-[(4-tert-Butyl-benzenesulfonyl)-methyl-amino]-ethyl}-4-oxo-3-p-tolyl-3,4-dihydro-quinazolin-6-yloxy)-acetic acid ethyl ester



The title compound was prepared in a manner similar to that described in example 53 by replacing benzyl alcohol with hydroxy-acetic acid ethyl ester. ^{1}H-NMR ($CDCl_3$): δ 7.56 (d, 1H), 7.50 (m, 2H), 7.44 (m, 2H), 7.33 (m, 1H), 7.24 (m, 4H), 7.05 (m, 1H), 4.93 (q, 1H), 4.03 (t, 2H), 3.15 (s, 3H), 2.48 (s, 3H), 1.79 (m, 2H), 1.5 (m, 2H), 1.28 (d, 1H), 1.18 (s, 9H), 0.98 (t, 3H); MS (ESI) 592 (MH^+).

EXAMPLE 57

Time Resolved Fluorescence Resonance Energy Transfer (TR-FRET) Assay

The FRET assay was performed by incubating 8 nM of GST-FXR-LBD, 8 nM of Europium-labeled anti-GST antibody (Wallac), 16 nM biotin-SRC-1 peptide [5'-biotin-CPSSHSSLTERHKILHRLLQEGSPS-CONH2], 20 nM APC-SA [allophycocyanin conjugated streptavidin] (Wallac) in FRET assay buffer (20 mM KH_2PO_4/K_2HPO_4 (pH 7.3), 150 mM NaCl, 2 mM CHAPS, 2 mM EDTA, 1 mM DTT) in the presence of the test compound(s) for 2-4 hours at room temperature. Data was collected using an LJL Analyst with readings at 615 nm and 665 nm.

EXAMPLE 58

FXR Co-Transfection Assay

The basic co-transfection protocol for measuring FXR activity is as follows. CV-1 African Green Monkey Kidney cells are plated 24 hours before transfection to achieve approximately 70-80 percent confluency. Cells are transfected with CMX-hFXR, CMX-RXRα, Luc12 reporter (ECREx7-Tk-Luciferase), and a CMX-β-Galactosidase expression vector. The transfection reagent used is DOTAP. Cells are incubated with the DOTAP/DNA mixture for 5 hours after which the cells are harvested and plated onto either 96 well or 384 well plates containing the appropriate concentration of test compound. The assay is allowed to continue for an additional 18-20 hours, after which the cells are lysed, and the luciferase activity is measured on a standard plate reader.

Results of Examples 57 and 58

Both the FXR/ECREx7 co-transfection assay (Example 58) and the TR-FRET assay (Example 57) can be used to establish the EC_{50}/IC_{50} values for potency and percent activity or inhibition for efficacy. Efficacy defines the activity of a compound relative to a high control (chenodeoxycholic acid, CDCA) or a low control (DMSO/vehicle). The dose response curves are generated from an 8 point curve with concentrations differing by ½ LOG units. Each point represents the

average of 4 wells of data from a 384 well plate. The curve for the data is generated by using the equation:

Y =, Bottom + (Top-Bottom)/(1 + 10^((LogEC50-X)*HillSlope))

The EC_{50}/IC_{50} is therefore defined as the concentration at which an agonist or antagonist elicits a response that is half way between the Top (maximum) and Bottom (baseline) values. The EC_{50}/IC_{50} values represented are the averages of at least 3 independent experiments. The determination of the relative efficacy or % control for an agonist is by comparison to the maximum response achieved by chenodeoxycholic acid that is measured individually in each dose response experiment.

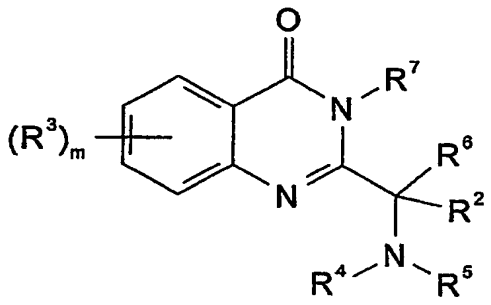
For the antagonist assay, 40 μM CDCA is added to each well of a 384 well plate to elicit a response. The % inhibition for each antagonist is therefore a measurement of the inhibition of the activity of 40 μM CDCA. In this example 100% inhibition would indicate that the activity of 40 μM CDCA has been reduced to baseline levels, defined as the activity of the assay in the presence of DMSO only.

Most of the compounds disclosed herein and tested exhibited activity in at least one of the above assays (EC_{50} or IC_{50} less than 10 μM). Most showed activity at below 1 μM. For example, 4-tert-Butyl-N-{1-[3-(4-methoxy-phenyl)-4-oxo-6-thiophen-2-yl-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide (Example 41) shows an EC_{50} of about 600 nM and a % efficacy of about 110% in the co-transfection assay; and 4-tert-Butyl-N-{1-[6-methoxy-3-(4-methoxy-phenyl)-4-oxo-3,4-dihydro-quinazolin-2-yl]-ethyl}-N-methyl-benzenesulfonamide (Example 27) shows an EC_{50} of about 300 nM and a % efficacy of about 190% in the co-transfection assay.

Since modifications will be apparent to those of skill in this art, it is intended that this invention be limited only by the scope of the appended claims.

WHAT IS CLAIMED IS:

1. A method of treating, preventing, or ameliorating the symptoms of a disease or disorder that is modulated or otherwise affected by nuclear receptor activity or in which nuclear receptor activity is implicated, comprising administering to a subject in need thereof an effective amount of a compound of formula I:



or a pharmaceutically acceptable derivative thereof, wherein:

R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{91} or $NR^{92}R^{93}$, with the proviso that R^7 is not 4-(1,1,1,3,3,3-hexafluoro-2-hydroxy-2-propyl)phenyl;

R^{91} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{92} and R^{93} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_jR^{94}$ where j is 1 or 2, and $C(M)R^{95}$, where M is selected from O and S; or R^{92} and R^{93} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{94} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{95} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{96} or $NR^{97}R^{98}$; R^{96} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{97} and R^{98} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted

cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

each R^3 is selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2; or any two R^3 groups, which substitute adjacent carbons on the ring, together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkylenedioxy, substituted or unsubstituted thioalkylenoxy, or substituted or unsubstituted alkylenedithioxy;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $C(D)R^{15}$ where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl, or R^{18} and R^{19} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or $C(D)R^{15}$ where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{12} or $NR^{10}R^{11}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl; or (ii) R^2 and R^6 together form substituted or unsubstituted alkylene or substituted or unsubstituted alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted

heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or

unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or

unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl,

substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 4, 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^2-R^7, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain

embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio,

hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

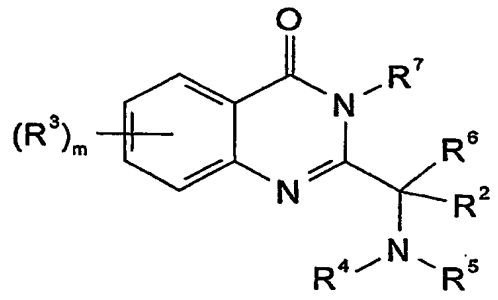
each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl,

arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or

alkylenedithioxy where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene.

2. The method of claim 1, wherein the disease or disorder is selected from hypercholesterolemia, hyperlipoproteinemia, hypertriglyceridemia, lipodystrophy, hyperglycemia, diabetes mellitus, dyslipidemia, atherosclerosis, gallstone disease, acne vulgaris, acneiform skin conditions, diabetes, Parkinson's disease, cancer, Alzheimer's disease, inflammation, immunological disorders, lipid disorders, obesity, conditions characterized by a perturbed epidermal barrier function, hyperlipidemia, cholestasis, peripheral occlusive disease, ischemic stroke, conditions of disturbed differentiation or excess proliferation of the epidermis or mucous membrane, and cardiovascular disorders.

3. A method of reducing cholesterol levels in a subject in need thereof, comprising administering an effective amount of a compound of formula I:



or a pharmaceutically acceptable derivative thereof, wherein:

R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{91} or $NR^{92}R^{93}$, with the proviso that R^7 is not 4-(1,1,1,3,3,3-hexafluoro-2-hydroxy-2-propyl)phenyl;

R^{91} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{92} and R^{93} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_jR^{94}$ where j is 1 or 2, and $C(M)R^{95}$, where M is selected from O and S; or R^{92} and R^{93} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{94} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{95} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{96} or $NR^{97}R^{98}$; R^{96} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or

unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{97} and R^{98} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

each R^3 is selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2; or any two R^3 groups, which substitute adjacent carbons on the ring, together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkylenedioxy, substituted or unsubstituted thioalkylenoxy, or substituted or unsubstituted alkylenedithioxy;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted

cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $C(D)R^{15}$ where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl, or R^{18} and R^{19} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl,

substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or C(D)R^{15} where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{12} or $NR^{10}R^{11}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or

unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl; or (ii) R^2 and R^6 together form substituted or unsubstituted alkylene or substituted or unsubstituted alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted

aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl,

substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 4, 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^2-R^7, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl,

alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

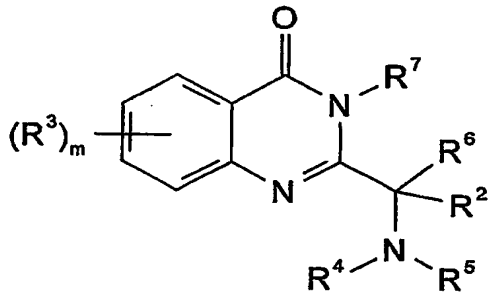
R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,

hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene.

4. A method of treating, preventing, or ameliorating one or more symptoms of a disease or disorder which is affected by cholesterol, triglyceride, or bile acid levels, comprising administering to a subject in need thereof an effective amount of a compound of formula I:



or a pharmaceutically acceptable derivative thereof, wherein:

R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or

unsubstituted heterocyclylalkyl, OR^{91} or $NR^{92}R^{93}$, with the proviso that R^7 is not 4-(1,1,1,3,3,3-hexafluoro-2-hydroxy-2-propyl)phenyl;

R^{91} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{92} and R^{93} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_jR^{94}$ where j is 1 or 2, and $C(M)R^{95}$, where M is selected from O and S; or R^{92} and R^{93} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{94} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{95} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or

unsubstituted heterocyclylalkyl, OR^{96} or $NR^{97}R^{98}$; R^{96} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{97} and R^{98} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

each R^3 is selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2; or any two R^3 groups, which substitute adjacent carbons on the ring, together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkylenedioxy, substituted or unsubstituted thioalkylenoxy, or substituted or unsubstituted alkylenedithioxy;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $C(D)R^{15}$ where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl, or R^{18} and R^{19} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or

unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or $C(D)R^{15}$ where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{12} or $NR^{10}R^{11}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl,

substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl; or (ii) R^2 and R^6 together form substituted or unsubstituted alkylene or substituted or unsubstituted alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or

unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each

independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or

unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 4, 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^2-R^7, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl,

arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

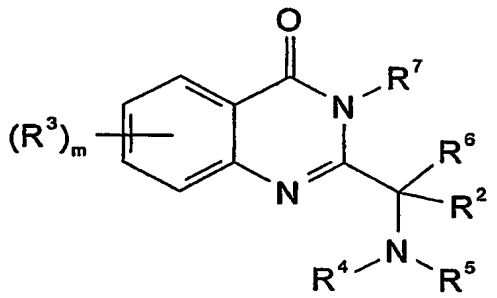
R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido,

$-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene.

5. A method of modulating nuclear receptor activity, comprising contacting the nuclear receptor with a compound of formula I:



or a pharmaceutically acceptable derivative thereof, wherein:

R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or

unsubstituted heterocyclylalkyl, OR^{91} or $NR^{92}R^{93}$, with the proviso that R^7 is not 4-(1,1,1,3,3,3-hexafluoro-2-hydroxy-2-propyl)phenyl;

R^{91} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{92} and R^{93} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_jR^{94}$ where j is 1 or 2, and $C(M)R^{95}$, where M is selected from O and S; or R^{92} and R^{93} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{94} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{95} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or

unsubstituted heterocyclylalkyl, OR^{96} or $NR^{97}R^{98}$; R^{96} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{97} and R^{98} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

each R^3 is selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2; or any two R^3 groups, which substitute adjacent carbons on the ring, together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkylenedioxy, substituted or unsubstituted thioalkylenoxy, or substituted or unsubstituted alkylenedithioxy;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $C(D)R^{15}$ where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl, or R^{18} and R^{19} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or

unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or $C(D)R^{15}$ where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{12} or $NR^{10}R^{11}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl,

substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl; or (ii) R^2 and R^6 together form substituted or unsubstituted alkylene or substituted or unsubstituted alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or

unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each

independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or

unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 4, 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^2-R^7, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl,

arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido,

$-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene.

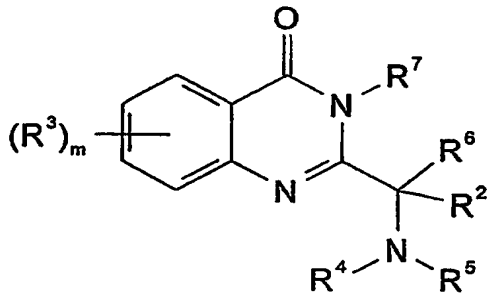
6. The method of claim 5, wherein the nuclear receptor is an orphan nuclear receptor.

7. The method of claim 5, wherein the nuclear receptor is farnesoid X receptor (FXR).

8. The method of any of claims 5-7, wherein the compound is a nuclear receptor agonist.

9. The method of any of claims 5-7, wherein the compound is a nuclear receptor antagonist.

10. A method of modulating cholesterol metabolism, comprising administering an effective amount of a compound of formula I:



or a pharmaceutically acceptable derivative thereof, wherein:

R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{91} or $NR^{92}R^{93}$, with the proviso that R^7 is not 4-(1,1,1,3,3,3-hexafluoro-2-hydroxy-2-propyl)phenyl;

R^{91} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{92} and R^{93} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_jR^{94}$ where j is 1 or 2, and $C(M)R^{95}$, where M is selected from O and S; or R^{92} and R^{93} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{94} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or

unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{95} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{96} or $NR^{97}R^{98}$; R^{96} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{97} and R^{98} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

each R^3 is selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2; or any two R^3 groups, which substitute

adjacent carbons on the ring, together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkylenedioxy, substituted or unsubstituted thioalkylenoxy, or substituted or unsubstituted alkylenedithioxy;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $C(D)R^{15}$ where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl, or R^{18} and R^{19} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or

unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or $C(D)R^{15}$ where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{12} or $NR^{10}R^{11}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl; or (ii) R^2 and R^6 together form substituted or unsubstituted alkylene or substituted or unsubstituted alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or

unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl,

substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or

unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 4, 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^2-R^7, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl,

diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^{+}R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

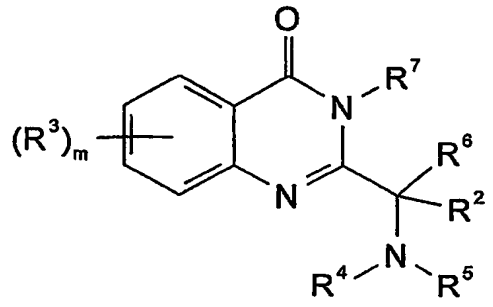
R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl,

alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene.

11. A method of treating, preventing or ameiliorating one or more symptoms of hypocholesterolemia in a subject in need thereof, comprising administering an effective amount of a compound of formula I:



or a pharmaceutically acceptable derivative thereof, wherein:

R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{91} or $NR^{92}R^{93}$, with the proviso that R^7 is not 4-(1,1,1,3,3,3-hexafluoro-2-hydroxy-2-propyl)phenyl;

R^{91} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{92} and R^{93} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_jR^{94}$ where j is 1 or 2, and $C(M)R^{95}$, where M is

selected from O and S; or R^{92} and R^{93} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{94} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{95} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{96} or $NR^{97}R^{98}$; R^{96} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{97} and R^{98} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

each R^3 is selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or

unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2; or any two R^3 groups, which substitute adjacent carbons on the ring, together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkylenedioxy, substituted or unsubstituted thioalkylenoxy, or substituted or unsubstituted alkylenedithioxy;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $C(D)R^{15}$ where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl,

aralkyl and heteroaralkyl, or R^{18} and R^{19} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or $C(D)R^{15}$ where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{12} or $NR^{10}R^{11}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl; or (ii) R^2 and R^6 together form substituted or unsubstituted alkylene or substituted or unsubstituted alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or

unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted

heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted

aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or

unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 4, 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^2-R^7, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl,

triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or

alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

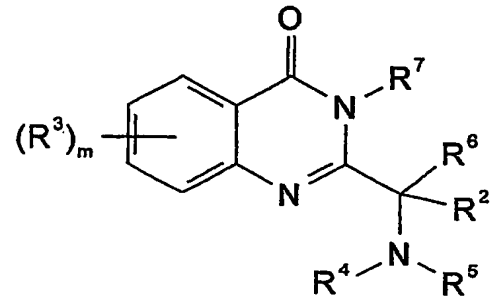
R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy,

alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene.

12. A method of increasing cholesterol efflux from cells of a subject, comprising administering an effective amount of a compound of formula I:



or a pharmaceutically acceptable derivative thereof, wherein:

R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{91} or $NR^{92}R^{93}$, with the proviso that R^7 is not 4-(1,1,1,3,3,3-hexafluoro-2-hydroxy-2-propyl)phenyl;

R^{91} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{92} and R^{93} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_jR^{94}$ where j is 1 or 2, and $C(M)R^{95}$, where M is

selected from O and S; or R^{92} and R^{93} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{94} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{95} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{96} or $NR^{97}R^{98}$; R^{96} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{97} and R^{98} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

each R^3 is selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or

unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2; or any two R^3 groups, which substitute adjacent carbons on the ring, together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkylenedioxy, substituted or unsubstituted thioalkylenoxy, or substituted or unsubstituted alkylenedithioxy;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $C(D)R^{15}$ where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl,

aralkyl and heteroaralkyl, or R^{18} and R^{19} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or $C(D)R^{15}$ where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{12} or $NR^{10}R^{11}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl; or (ii) R^2 and R^6 together form substituted or unsubstituted alkylene or substituted or unsubstituted alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or

unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted

heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted

aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or

unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 4, 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^2-R^7, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl,

triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or

alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

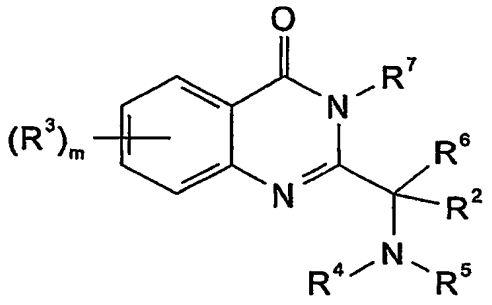
R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy,

alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene.

13. A method of increasing the expression of ATP-Binding Cassette (ABC1) in the cells of a subject, comprising administering an effective amount of a compound of formula I:



or a pharmaceutically acceptable derivative thereof, wherein:

R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{91} or $NR^{92}R^{93}$, with the proviso that R^7 is not 4-(1,1,1,3,3,3-hexafluoro-2-hydroxy-2-propyl)phenyl;

R^{91} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{92} and R^{93} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_jR^{94}$ where j is 1 or 2, and $C(M)R^{95}$, where M is

selected from O and S; or R^{92} and R^{93} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{94} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{95} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{96} or $NR^{97}R^{98}$; R^{96} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{97} and R^{98} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

each R^3 is selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or

unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2; or any two R^3 groups, which substitute adjacent carbons on the ring, together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkylenedioxy, substituted or unsubstituted thioalkylenoxy, or substituted or unsubstituted alkylenedithioxy;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $C(D)R^{15}$ where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl,

aralkyl and heteroaralkyl, or R^{18} and R^{19} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or $C(D)R^{15}$ where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{12} or $NR^{10}R^{11}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl; or (ii) R^2 and R^6 together form substituted or unsubstituted alkylene or substituted or unsubstituted alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or

unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted

heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted

aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or

unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 4, 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^2-R^7, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl,

triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or

alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

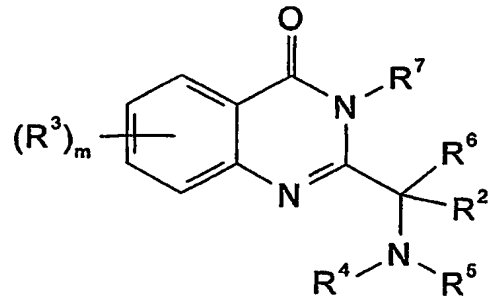
R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy,

alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfjnyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene.

14. An *in vitro* method for altering nuclear receptor activity, comprising contacting the nuclear receptor with a compound of formula I:



or a pharmaceutically acceptable derivative thereof, wherein:

R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{91} or $NR^{92}R^{93}$, with the proviso that R^7 is not 4-(1,1,1,3,3,3-hexafluoro-2-hydroxy-2-propyl)phenyl;

R^{91} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{92} and R^{93} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_jR^{94}$ where j is 1 or 2, and $C(M)R^{95}$, where M is

selected from O and S; or R^{92} and R^{93} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{94} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{95} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{96} or $NR^{97}R^{98}$; R^{96} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{97} and R^{98} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

each R^3 is selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or

unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2; or any two R^3 groups, which substitute adjacent carbons on the ring, together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkylenedioxy, substituted or unsubstituted thioalkylenoxy, or substituted or unsubstituted alkylenedithioxy;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $C(D)R^{15}$ where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl,

aralkyl and heteroaralkyl, or R^{18} and R^{19} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or $C(D)R^{15}$ where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{12} or $NR^{10}R^{11}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl; or (ii) R^2 and R^6 together form substituted or unsubstituted alkylene or substituted or unsubstituted alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or

unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted

heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted

aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or

unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 4, 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^2-R^7, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl,

triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^{+}R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or

alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy,

alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene.

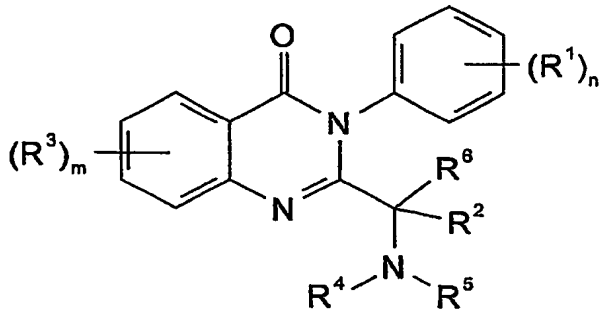
15. The method of any of claims 1-14, wherein R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, or substituted or unsubstituted aralkyl.

16. The method of any of claims 1-15, wherein R^7 is hydrogen, substituted or unsubstituted alkyl, aryl, or aralkyl.

17. The method of any of claims 1-16, wherein R^7 is hydrogen, methyl, ethyl, propyl, 2-methoxyethyl, substituted or unsubstituted phenyl, benzyl, or naphthyl.

18. The method of any of claims 1-17, wherein R^7 is substituted or unsubstituted phenyl, and is selected with the proviso that it is not substituted at the 4-position with $-C(OH)(CF_3)_2$.

19. The method of any of claims 1-18, wherein the compound has formula II:



or a pharmaceutically acceptable derivative thereof, wherein:

each R^1 and R^3 are independently selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2, with the proviso that R^1 is not 4-$C(OH)(CF_3)_2$; or any two R^1 groups or R^3 groups, which substitute adjacent carbons on the ring, together form, together with the atoms to which they are attached, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

n is an integer from 0 to 5;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $C(D)R^{15}$ where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl, or R^{18} and R^{19} together for alkylene, alkenylene or alkyleneoxyalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or $C(D)R^{15}$ where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen or substituted or unsubstituted alkyl; or (ii) R^2 and R^6 together form alkylene or alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or

unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or

unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted

heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^1-R^6, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl,

aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy,

alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene.

20. The method of claim 19, wherein R^1 is not $-C(OH)(CF_3)_2$.

21. The method of any of claims 1-20, wherein R^6 is hydrogen.

22. The method of any of claims 1-21, wherein n is 0, 1 or 2.

23. The method of any of claims 1-22, wherein m is 1.

24. The method of any of claims 19-23, wherein each R^1 is independently halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted dialkylamino, substituted or unsubstituted aralkoxy, hydroxy, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclyl or substituted or unsubstituted cycloalkyl.

25. The method of any of claims 19-24, wherein each R^1 is independently halo; pseudohalo; alkyl; haloalkyl; alkoxy; haloalkoxy; heterocyclylalkoxy; alkoxyalkoxy; aryl; aryl substituted with alkyl, halo, -COOH, alkoxy, pseudohalo or -COO-alkyl; dialkylamino; aralkoxy; hydroxy; heteroaryl; heterocyclyl; or cycloalkyl.

26. The method of any of claims 19-25, wherein each R^1 is independently chloro, fluoro, ethyl, methyl, methoxy, bromo, cyano, phenyl, tert-butyl, trifluoromethoxy, dimethylamino, trifluoromethyl, benzyloxy, hydroxy, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, ethoxy, isopropoxy, butoxy, isobutoxy, 2-(N-morpholino)ethoxy, 2-methoxyethoxy, 4-cyanophenyl, 2-

thienyl, 3-thienyl, 3-methoxycarbonylphenyl, 4-methoxycarbonylphenyl, 3-hydroxycarbonylphenyl, N-pyrrolidinyl, or N-morpholinyl.

27. The method of any of claims 1-26, wherein R^2 is hydrogen or substituted or unsubstituted alkyl, and R^6 is hydrogen.

28. The method of any of claims 1-27, wherein R^2 is hydrogen or alkyl.

29. The method of any of claims 1-28, wherein R^2 is hydrogen, methyl or ethyl.

30. The method of any of claims 1-29, wherein each R^3 is independently substituted or unsubstituted alkyl, halo, pseudohalo, substituted or unsubstituted alkoxy, hydroxy, substituted or unsubstituted aralkoxy, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclyl, or substituted or unsubstituted cycloalkyl.

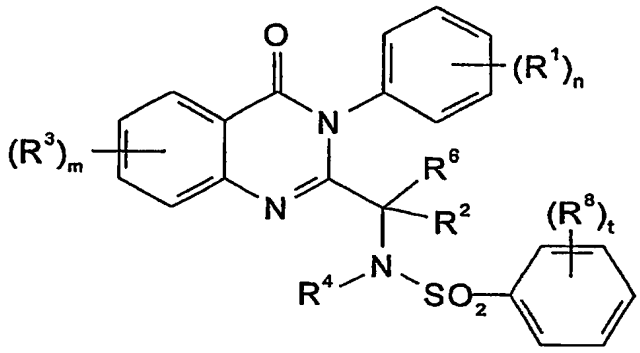
31. The method of any of claims 1-30, wherein each R^3 is independently alkyl; halo; alkoxy; hydroxy; aralkoxy; aryl; heteroaryl; alkoxycarbonylalkoxy; aryl substituted with alkyl, halo, pseudohalo, alkoxy, -COOH or -COO-alkyl; or heterocyclyl.

32. The method of any of claims 1-31, wherein each R^3 is independently methyl, chloro, methoxy, hydroxy, bromo, ethoxy, isopropoxy, isobutoxy, butoxy, benzyloxy, ethoxycarbonylmethoxy, phenyl, 2-thienyl, 3-thienyl, 2-methylphenyl, 3-methylphenyl, 4-methylpheny, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3-methoxyphenyl, 4-methoxyphenyl, 4-hydroxycarbonylphenyl, N-pyrrolidinyl, N-morpholinyl, 3-methoxycarbonylphenyl, 4-methoxycarbonylphenyl, 3-hydroxycarbonylphenyl, 4-cyanophenyl, or piperidinyl.

33. The method of any of claims 1-32, wherein one of R^4 and R^5 is $-SO_2-$(substituted or unsubstituted aryl).

34. The method of any of claims 1-33, wherein one of R^4 and R^5 is $-SO_2-$(substituted or unsubstituted phenyl).

35. The method of any of claims 1-34, wherein the compound has formula III:



or a pharmaceutically acceptable derivative thereof, wherein R^1, R^2, R^3, R^4, R^6, n and m are as defined above; t is an integer from 0 to 5; each R^8 is independently substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted heteroaryl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, halo, pseudohalo; or any two R^8 substituents, which substitute adjacent atoms on the ring, together form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl ring having 5 or 6 members in the ring and where the heteroatoms, if present, are selected from O, S and substituted or unsubstituted N; where R^8, when substituted, is substituted with one or more, in one embodiment one to five, in another embodiment one, two or three, substituents each independently selected from Q^1, as defined above.

36. The method of claim 35, wherein any two R^8 groups, which substitute adjacent carbons on the ring, together form $-N=CR^{70}-CR^{70}=CR^{70}-$ or $-CR^{70}=CR^{70}-CR^{70}=CR^{70}-$, where each R^{70} is independently hydrogen, halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or

unsubstituted heteroaryl, substituted or unsubstituted aralkyl, or substituted or unsubstituted heteroaralkyl;

where R^8 and R^{70}, when substituted, are substituted with one or more, in one embodiment one to five, in another embodiment one, two or three, substituents each independently selected from Q^1, as defined above.

37. The method of claim 35, wherein each R^8 is independently alkyl, alkoxy, haloalkoxy, heterocyclyl, heteroaryl, halo, haloalkyl, aryl or pseudohalo; or any two R^8 groups, which substitute adjacent carbons on the ring, together form -N=CH-CH=CH- or -CH=CH-CH=CH-.

38. The method of any of claims 35-37, wherein each R^8 is independently tert-butyl, methoxy, methyl, trifluoromethoxy, 2-thienyl, fluoro, chloro, trifluoromethyl, phenyl, cyano, n-propyl, 1,1-dimethylpropyl, isopropyl, butoxy or n-butyl; or any two R^8 groups, which substitute adjacent carbons on the ring, together form -N=CH-CH=CH- or -CH=CH-CH=CH-.

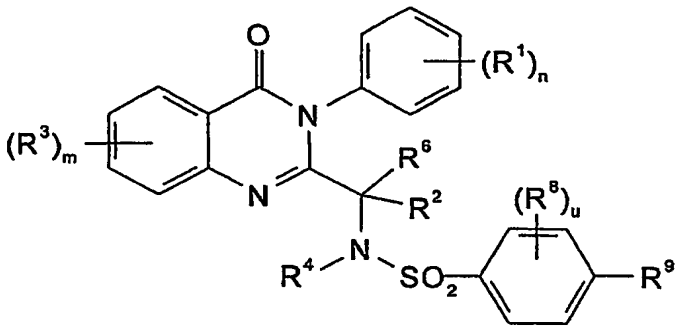
39. The method of any of claims 33-38, wherein R^4 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, or substituted or unsubstituted heteroaralkyl.

40. The method of any of claims 33-39, wherein R^4 is hydrogen, alkyl, aralkyl or heteroaralkyl.

41. The method of any of claims 33-40, wherein R^4 is hydrogen, methyl, 2-methoxy-1-ethyl, propyl, isobutyl, butyl, pentyl, isopentyl, hexyl, benzyl, phenethyl or 2-thienylmethyl.

42. The method of any of claims 35-41, wherein one R^8 group is 4-tert-butyl or 4-isopropyl.

43. The method of any of claims 35-42, wherein the compound has formula IV:



or a pharmaceutically acceptable derivative thereof, wherein R^1, R^2, R^3, R^4, R^6, R^8, m and n are selected as above; u is an integer from 0 to 4; and R^9 is tert-butyl or isopropyl.

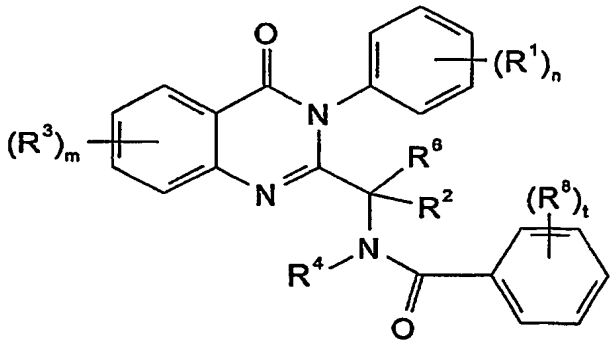
44. The method of claim 43, wherein R^9 is tert-butyl.

45. The method of claim 43, wherein R^9 is isopropyl.

46. The method of any of claims 1-32, wherein one of R^4 and R^5 is -C(O)-(substituted or unsubstituted aryl).

47. The method of any of claims 1-32 and 46, wherein one of R^4 and R^5 is -C(O)-(substituted or unsubstituted phenyl).

48. The method of any of claims 1-32, 46 and 47, wherein the compound has formula V:



or a pharmaceutically acceptable derivative thereof, wherein R^1, R^2, R^3, R^4, R^6, R^8, t, n and m are as defined above.

49. The method of any of claims 46-48, wherein each R^1 is independently halo, substituted or unsubstituted alkyl, or substituted or

unsubstituted alkoxy, where the substituents, when present, are each independently selected from Q^1, as defined above.

50. The method of any of claims 46-49, wherein each R^1 is independently alkoxy, alkyl or halo.

51. The method of any of claims 46-50, wherein each R^1 is independently methoxy, methyl, chloro or fluoro.

52. The method of any of claims 46-51, wherein R^2 is hydrogen or substituted or unsubstituted alkyl, where the substituents, when present, are each independently selected from Q^1, as defined above.

53. The method of any of claims 46-52, wherein R^2 is hydrogen or alkyl.

54. The method of any of claims 46-53, wherein R^2 is hydrogen or methyl.

55. The method of any of claims 46-54, wherein each R^3 is independently hydrogen or substituted or unsubstituted alkoxy, where the substituents, when present, are each independently selected from Q^1, as defined above.

56. The method of any of claims 46-55, wherein each R^3 is independently hydrogen or alkoxy.

57. The method of any of claims 46-56, wherein each R^3 is independently hydrogen or methoxy.

58. The method of any of claims 46-57, wherein R^4 is substituted or unsubstituted alkyl, where the substituents, when present, are each independently selected from Q^1, as defined above.

59. The method of any of claims 46-58, wherein R^4 is alkyl.

60. The method of any of claims 46-59, wherein R^4 is methyl or butyl.

61. The method of any of claims 46-60, wherein R^6 is hydrogen.

62. The method of any of claims 46-61, wherein each R^8 is independently substituted or unsubstituted alkyl, where the substituents,

when present, are each independently selected from Q^1, as defined above.

63. The method of any of claims 46-62, wherein each R^8 is alkyl.

64. The method of any of claims 46-63, wherein R^8 is tert-butyl.

65. The method of any of claims 1-32, wherein one of R^4 and R^5 is -C(O)-(substituted or unsubstituted alkyl), where the substituents, when present, are each independently selected from Q^1, as defined above.

66. The method of any of claims 1-32 and 65, wherein one of R^4 and R^5 is -C(O)-alkyl.

67. The method of any of claims 1-32, 65 and 66, wherein one of R^4 and R^5 is -C(O)-octyl.

68. The method of any of claims 1-32, wherein one of R^4 and R^5 is $-C(O)-NR^{80}R^{81}$, where R^{80} and R^{81} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; or R^{80} and R^{81} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; where R^{80} and R^{81} are each independently unsubstituted or substituted with one or more, in one embodiment one to five, in another embodiment one, two or three, substituents each independently selected from Q^1, as defined above.

69. The method of claim 68, wherein R^{80} and R^{81} are each independently selected from hydrogen, substituted or unsubstituted cycloalkyl, and substituted or unsubstituted aryl.

70. The method of claim 68 or claim 69, wherein R^{80} is hydrogen.

71. The method of any of claims 68-69, wherein R^{81} is cyclohexyl, 4-nitrophenyl, 2-methoxyphenyl, 3-cyanophenyl, 3,4-dichlorophenyl, 2,6-diisopropylphenyl, 2-methylphenyl, 2-trifluoromethylphenyl, 2-fluorophenyl, 3-fluorophenyl, 3-methylphenyl, 3-chlorophenyl, 2,6-dimethylphenyl or 3-trifluoromethylphenyl.

72. The method of any of claims 1-32, wherein R^4 and R^5 together form substituted or unsubstituted alkyleneazaalkylene, where the substituents, if present, are each independently selected from Q^1, as defined above.

73. The method of any of claims 1-32 and 72, wherein R^4 and R^5 together form $-CH_2-CHMe-N(R^{90})-CH_2-CH_2-$, where R^{90} is substituted or unsubstituted heteroarylcarbonyl, substituted or unsubstituted alkylcarbonyl, substituted or unsubstituted arylcarbonyl, substituted or unsubstituted arylsulfonyl, substituted or unsubstituted alkylaminocarbonyl, or substituted or unsubstituted arylaminocarbonyl.

74. The method of claim 73, wherein R^{90} is 2-thienylcarbonyl, butyryl, 4-fluorobenzoyl, benzyloxyacetyl, diphenylacetyl, 4-nitrobenzoyl, 2,5-dichlorobenzenesulfonyl, tert-butylaminocarbonyl, phenylaminocarbonyl, 2,3-dichlorophenylaminocarbonyl, 4-tert-butylphenylsulfonyl or 3,4-methylenedioxybenzoyl.

75. The method of any of claims 1-74, wherein Q^2 is halo, pseudohalo, aralkoxy or nitro; or any two Q^2 groups, which substitute adjacent carbons, together form alkylenedioxy.

76. The method of any of claims 1-75, wherein Q^2 is nitro, fluoro, benzyloxy or chloro; or two Q^2 groups, which substitute adjacent carbons, together form methylenedioxy.

77. The method of any of claims 1-14, wherein the compound is selected from the compounds of any of Figures 1, 2 or 3.

78. A compound selected from the compounds of Figure 2.

79. A pharmaceutical composition, comprising a compound of claim 78 and a pharmaceutically acceptable carrier.

80. The pharmaceutical composition of claim 79 that is formulated for single dosage administration.

81. A compound of any of Examples 1-56.

82. A pharmaceutical composition, comprising the compound of claim 81 and a pharmaceutically acceptable carrier.

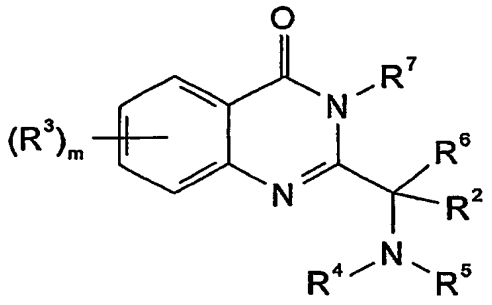
83. The pharmaceutical composition of claim 82 that is formulated for single dosage administration.

84. The method of any of claims 1-14, wherein the compound is selected from the compounds of any of Examples 1-56.

85. The method of any of claims 1-78 and 84, wherein a second active agent selected from antihyperlipidemic agents, plasma HDL-raising agents, antihypercholesterolemic agents, cholesterol biosynthesis inhibitors (such as HMG CoA reductase inhibitors, such as lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin and rivastatin), acyl-coenzyme A:cholesterol acytransferase (ACAT) inhibitors, probucol, raloxifene, nicotinic acid, niacinamide, cholesterol absorption inhibitors, bile acid sequestrants (such as anion exchange resins, or quaternary amines (*e.g.*, cholestyramine or colestipol)), low density lipoprotein receptor inducers, clofibrate, fenofibrate, benzofibrate, cipofibrate, gemfibrizol, vitamin B_6, vitamin B_{12}, anti-oxidant vitamins, β-blockers, anti-diabetes agents, angiotensin II antagonists, angiotensin converting enzyme inhibitors, platelet aggregation inhibitors, fibrinogen receptor antagonists, aspirin and fibric acid derivatives; is administered simultaneously with, prior to, or after administration of the compound.

86. A pharmaceutical composition, comprising, in a pharmaceutically acceptable carrier:

(i) a compound of formula I:



or a pharmaceutically acceptable derivative thereof, wherein:

R^7 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl, with the proviso that R^7 is not 4-(1,1,1,3,3,3-hexafluoro-2-hydroxy-2-propyl)phenyl;

each R^3 is selected from halo, pseudohalo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{10}R^{11}$, OR^{12}, $C(E)R^{13}$ where E is O, S or NR^{20}, or $S(O)_yR^{14}$ where y is 0, 1 or 2; or any two R^3 groups, which substitute adjacent carbons on the ring, together form alkylene, alkenylene, alkylenedioxy, thioalkylenoxy, or alkylenedithioxy;

n is an integer from 0 to 5;

m is an integer from 0 to 4;

R^{10} and R^{11} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, C(D)R^{15} where D is O or S, and $S(O)_wR^{16}$ where w is 1 or 2; R^{15} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; where R^{17} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; and R^{18} and R^{19} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl, or R^{18} and R^{19} together for alkylene, alkenylene or alkyleneoxyalkylene; R^{16} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{17} or $NR^{18}R^{19}$; or R^{10} and R^{11} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene;

R^{12} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl,

substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl or $C(D)R^{15}$ where D is O or S;

R^{13} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{14} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OH, OR^{17} or $NR^{18}R^{19}$;

R^{20} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^2, R^4, R^5 and R^6 are selected from (a) and (b) as follows:

(a) R^2 and R^6 are selected from (i) and (ii) as follows: (i) R^2 and R^6 are each independently hydrogen or substituted or unsubstituted alkyl; or (ii) R^2 and R^6 together form alkylene or alkenylene;

R^4 and R^5 are selected from (i) and (ii) as follows: (i) R^4 and R^5 are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted

alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $NR^{30}R^{31}$, OR^{32}, $S(O)_zR^{34}$ where z is 1 or 2, $BR^{35}R^{36}$, $PR^{37}R^{38}$, $P(O)R^{39}R^{40}$ and $C(G)R^{33}$, where G is selected from O, S and NR^{45}; or (ii) R^4 and R^5 together form substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkyleneoxyalkylene or substituted or unsubstituted alkyleneazaalkylene;

R^{30} and R^{31} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, $S(O)_wR^{46}$ where w is 1 or 2, and $C(J)R^{47}$, where J is selected from O and S; or R^{30} and R^{31} together form alkylene, alkenylene, alkyleneoxyalkylene or alkyleneazaalkylene; R^{46} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{47} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted

heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{48} or $NR^{49}R^{50}$; R^{48} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{49} and R^{50} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{32} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{34} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{51} or $NR^{52}R^{53}$; R^{51} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or

unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{52} and R^{53} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

R^{35}, R^{36}, R^{37}, R^{38}, R^{39} and R^{40} are each independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{54} and $NR^{55}R^{56}$; R^{54}, R^{55} and R^{56} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl;

R^{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or

unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, OR^{57}, $NR^{58}R^{59}$, $NR^{60}NR^{58}R^{59}$; R^{57} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl; R^{58}, R^{59} and R^{60} are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, and substituted or unsubstituted heterocyclylalkyl; and

R^{45} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkylalkyl, or substituted or unsubstituted heterocyclylalkyl;

(b) R^2 and R^5, or R^2 and R^4, or R^6 and R^5, or R^6 and R^4, together form a 5, 6 or 7 membered substituted or unsubstituted heterocyclyl group, or a 5 or 6 membered substituted or unsubstituted heteroaryl group; and the remainder of R^2, R^4, R^5 and R^6 are each independently selected as in (i) above;

each of R^2-R^7, R^{10}-R^{20}, R^{30}-R^{40}, R^{45}-R^{60}, when substituted, are substituted with one or more, in one embodiment one to five, in certain embodiments one or two, substituents each independently selected from Q^1, where Q^1 is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$,

dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q^1 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^1 groups, which substitute the same atom, together form alkylene;

R^{61}, R^{62} and R^{63} are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R^{64} is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$, where R^{67} and R^{68} are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R^{67} and R^{68} together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R^{65} is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

R^{66} is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or $-NR^{67}R^{68}$;

each Q^1 is independently unsubstituted or substituted with one or more substituents, in one embodiment one, two or three substituents, each independently selected from Q^2;

each Q^2 is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl,

aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^{+}R^{61}R^{62}R^{63}$, $P(R^{64})_2$, $P(=O)(R^{64})_2$, $OP(=O)(R^{64})2$, $-NR^{65}C(=O)R^{66}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or

alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene; and

(ii) one or more of a second active agent selected from antihyperlipidemic agents, plasma HDL-raising agents, antihypercholesterolemic agents, cholesterol biosynthesis inhibitors (such as HMG CoA reductase inhibitors, such as lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin and rivastatin), acyl-coenzyme A:cholesterol acytransferase (ACAT) inhibitors, probucol, raloxifene, nicotinic acid, niacinamide, cholesterol absorption inhibitors, bile acid sequestrants (such as anion exchange resins, or quaternary amines (*e.g.*, cholestyramine or colestipol)), low density lipoprotein receptor inducers, clofibrate, fenofibrate, benzofibrate, cipofibrate, gemfibrizol, vitamin B_6, vitamin B_{12}, anti-oxidant vitamins, β-blockers, anti-diabetes agents, angiotensin II antagonists, angiotensin converting enzyme inhibitors, platelet aggregation inhibitors, fibrinogen receptor antagonists, aspirin and fibric acid derivatives.

87. The method of claim 19, wherein any two R^1 or R^3 groups, which substitute adjacent carbons on the ring, together form alkylene, alkenylene, alkylenedioxy, thioalkylenoxy, or alkylenedithioxy.

ABSTRACT

Compounds, compositions and methods for modulating the activity of nuclear receptors are provided. In particular, quinazolinones are provided for modulating the activity of farnesoid X receptor (FXR) and/or orphan nuclear receptors.

Applicants: Martin *et al.*
Title: QUINAZOLINONE ODULATORS OF NUCLEAR RECEPTORS
Filed: March 7, 2002
Atty. Docket No.: 38205-P3002

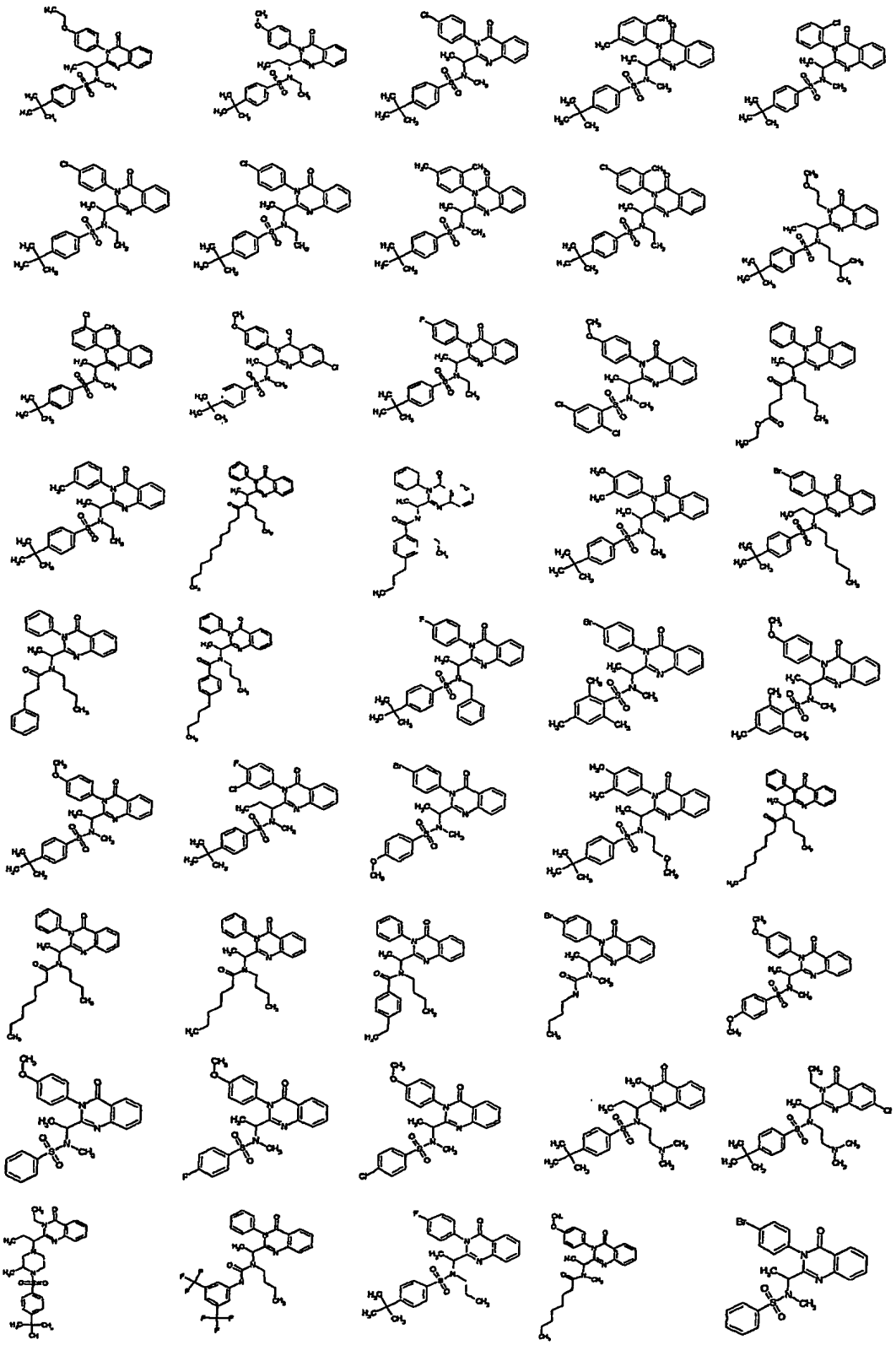


Figure 1

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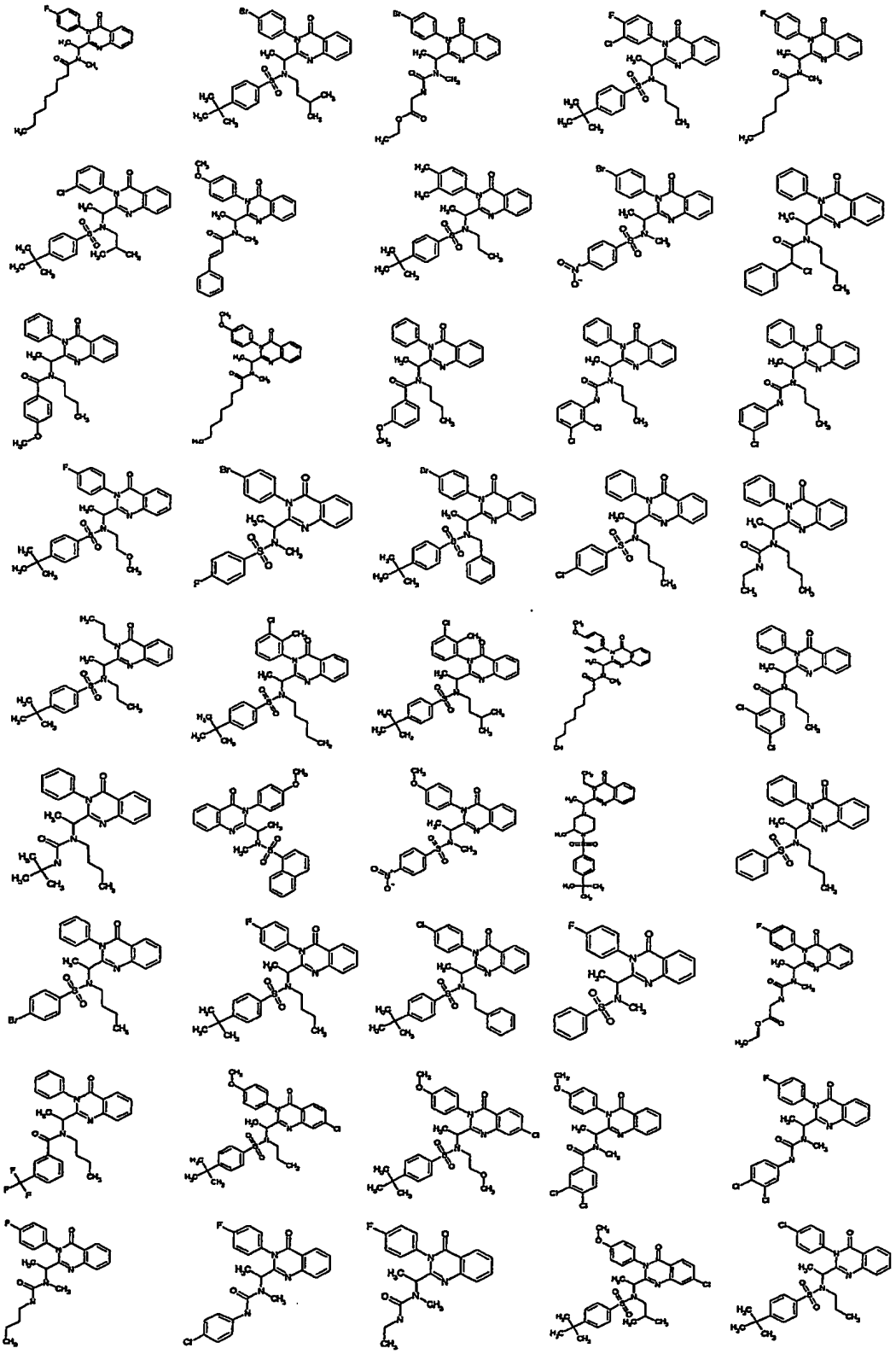

Figure 1

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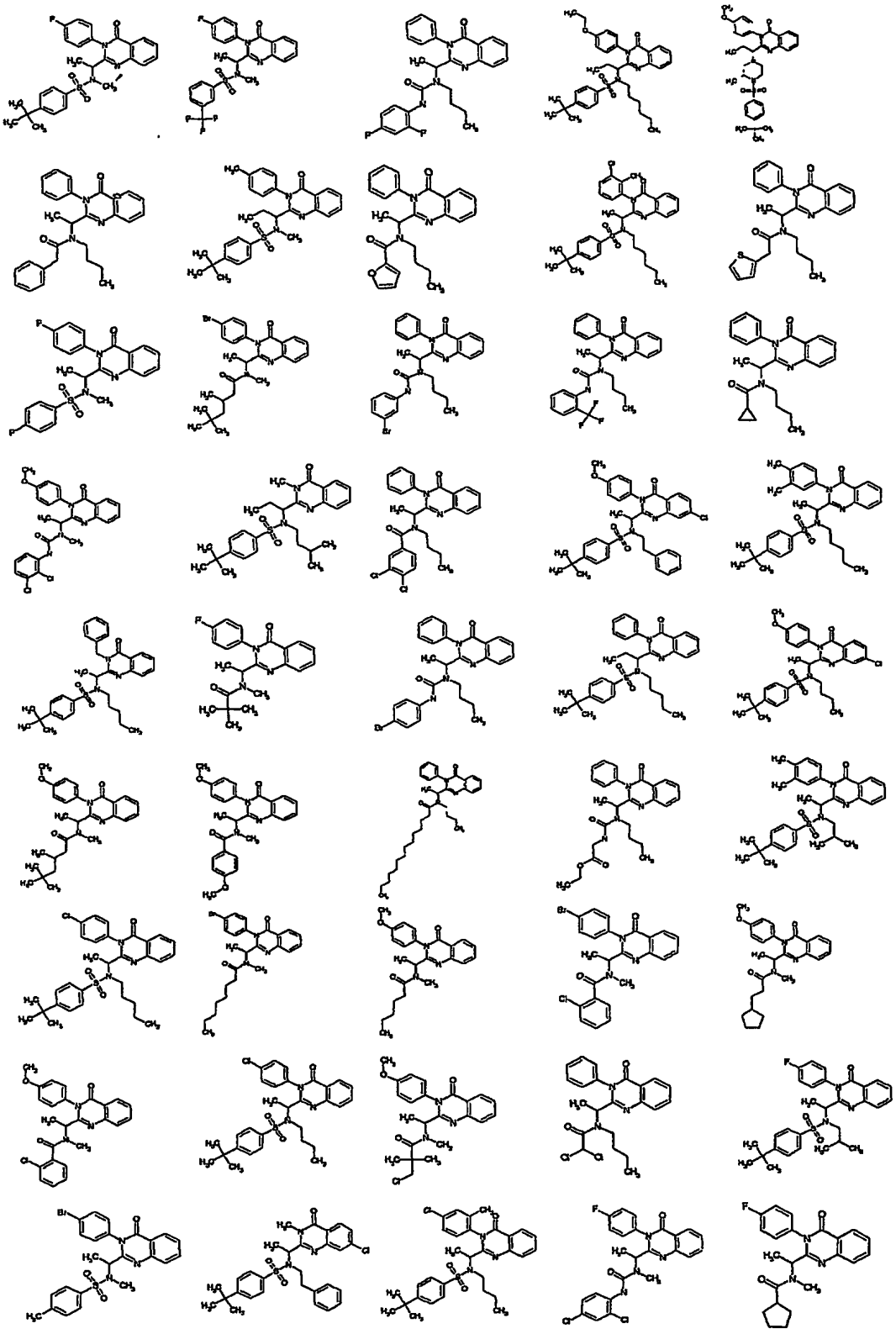

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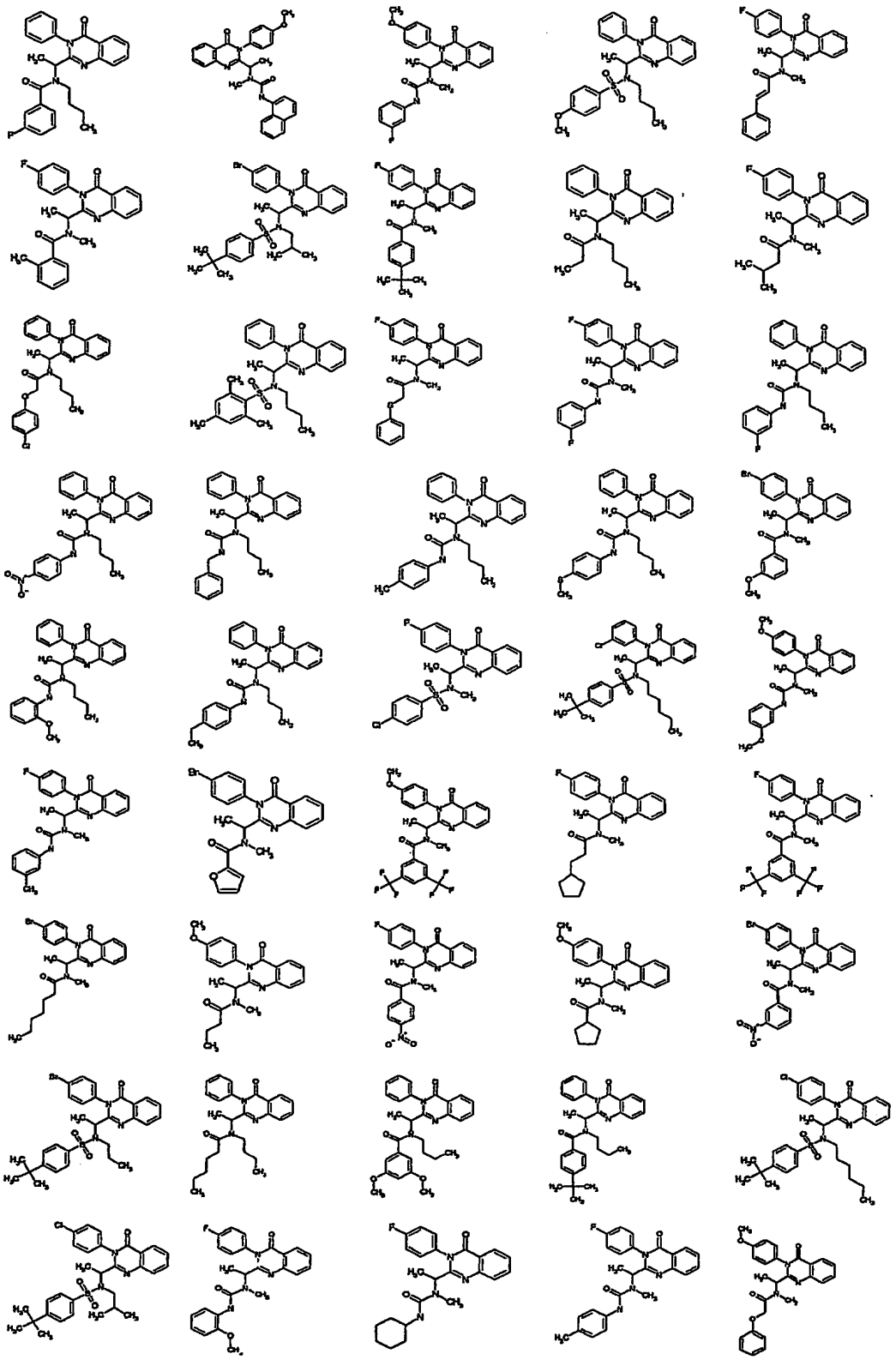

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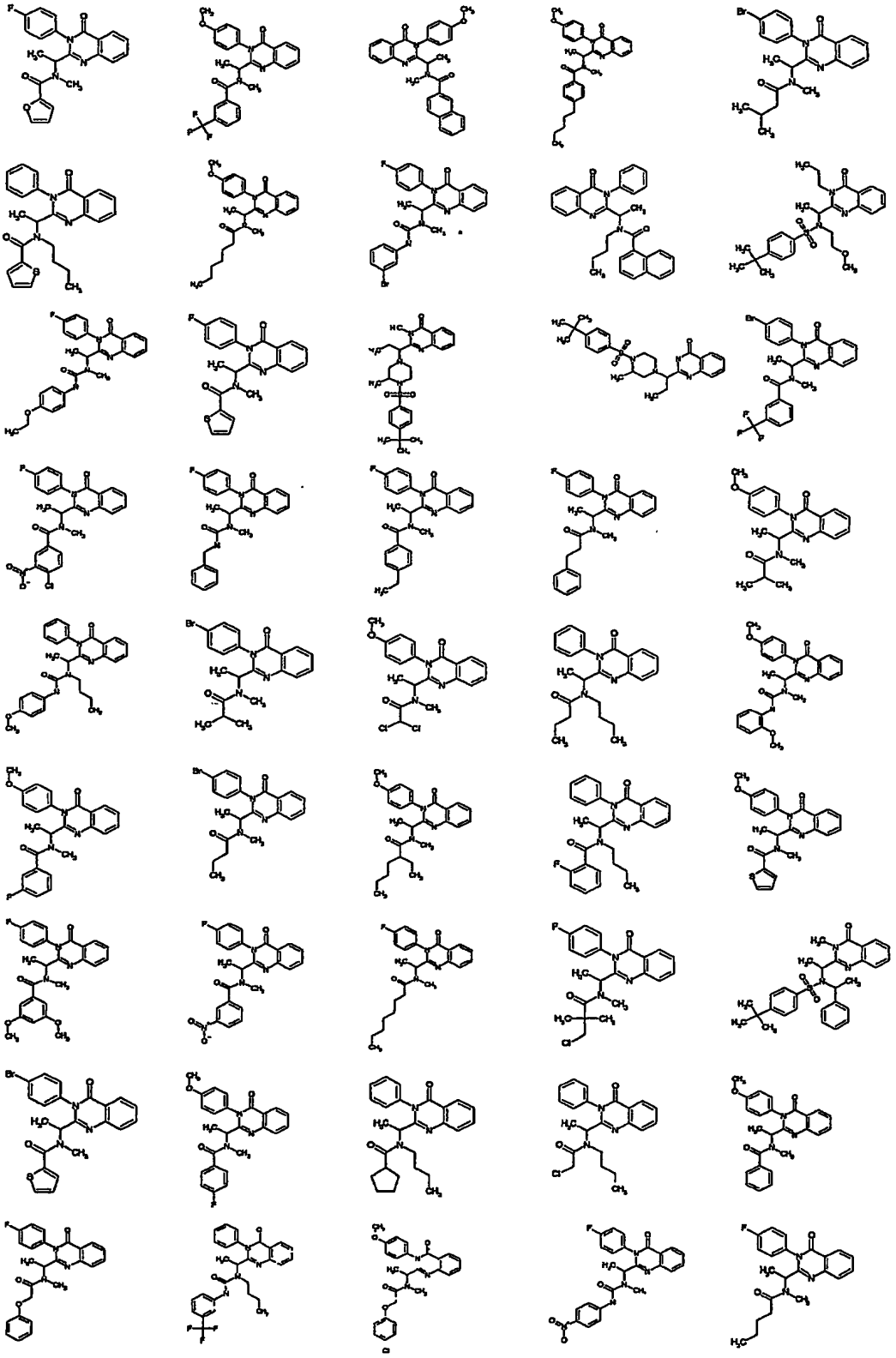

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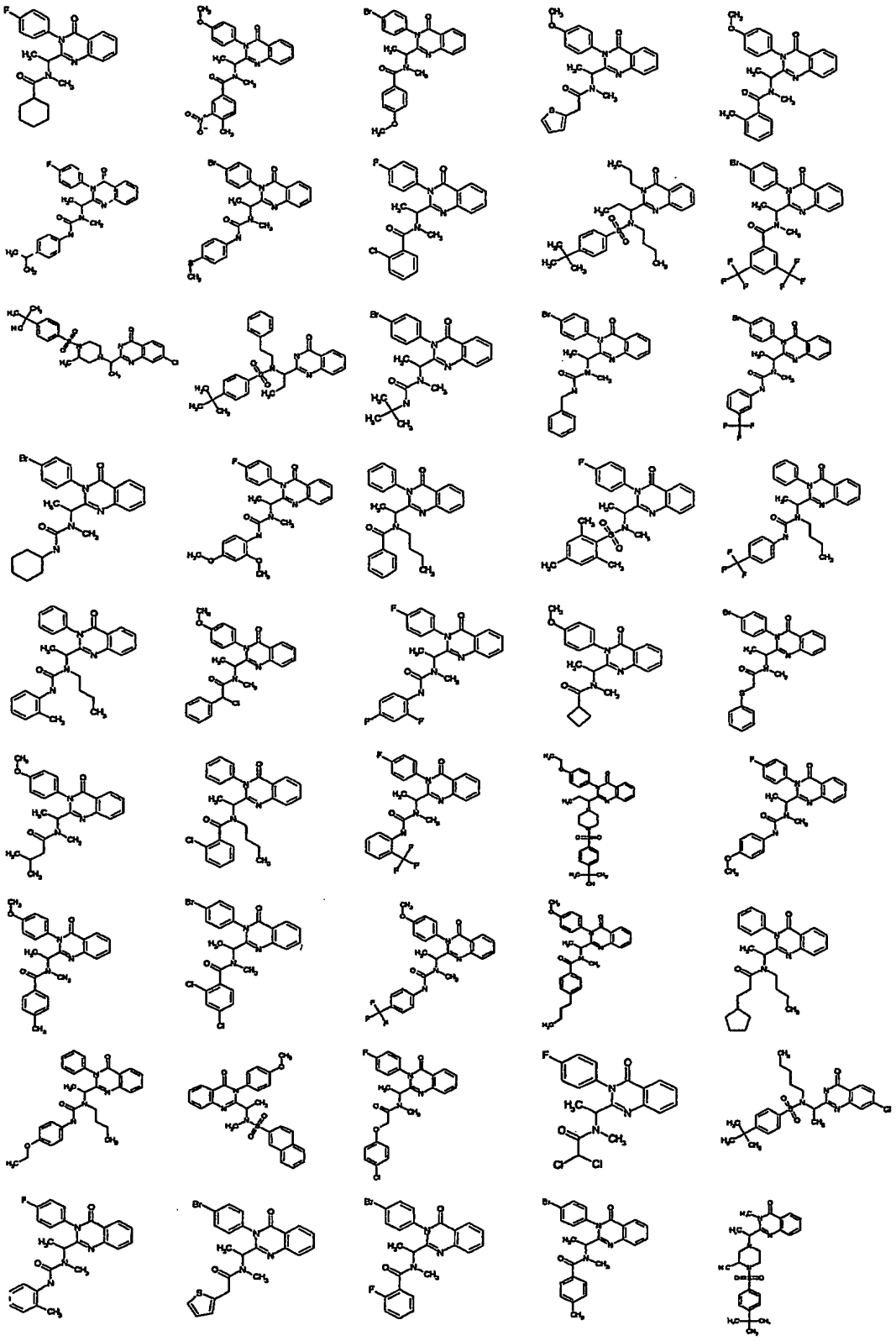

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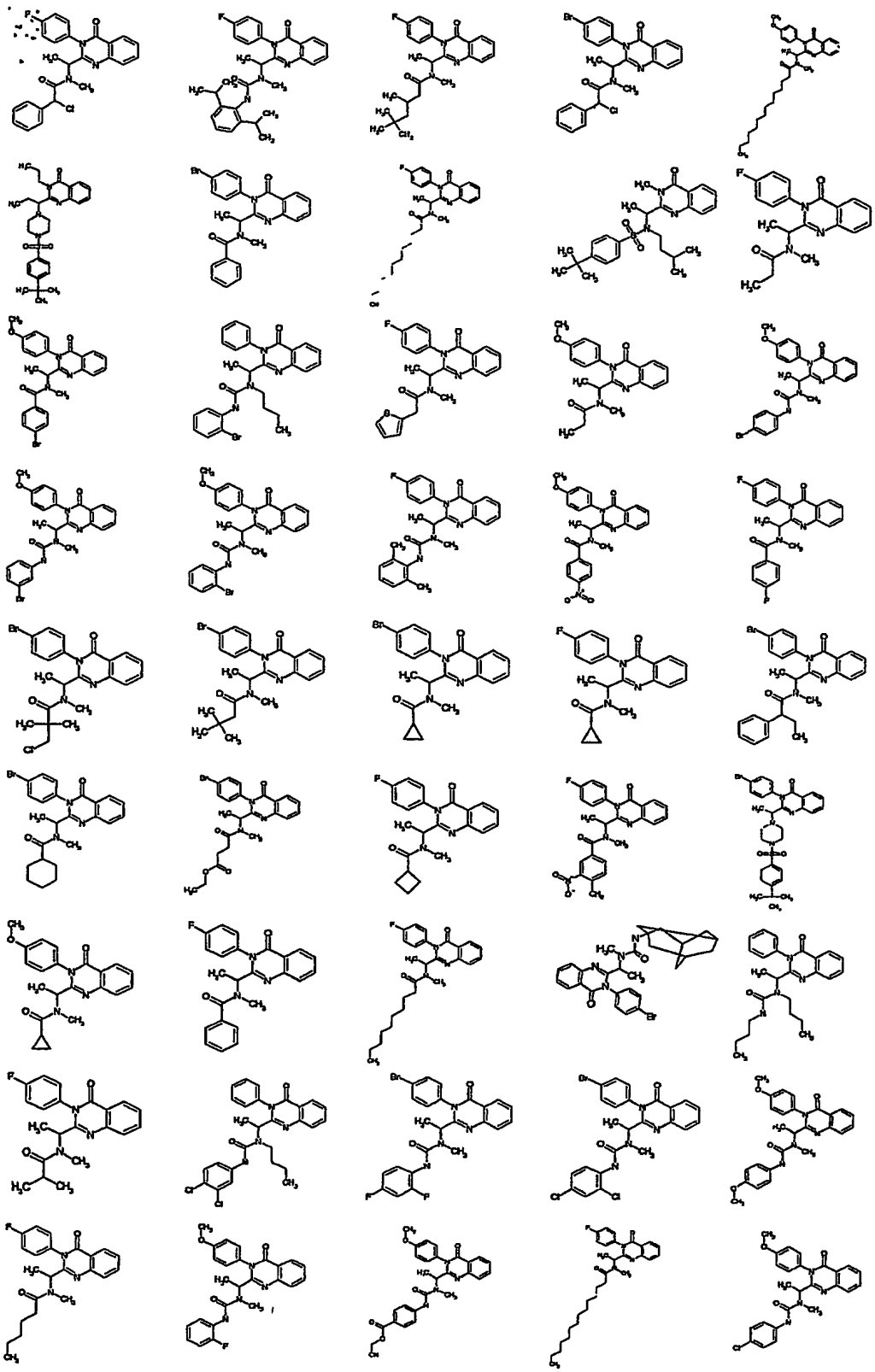

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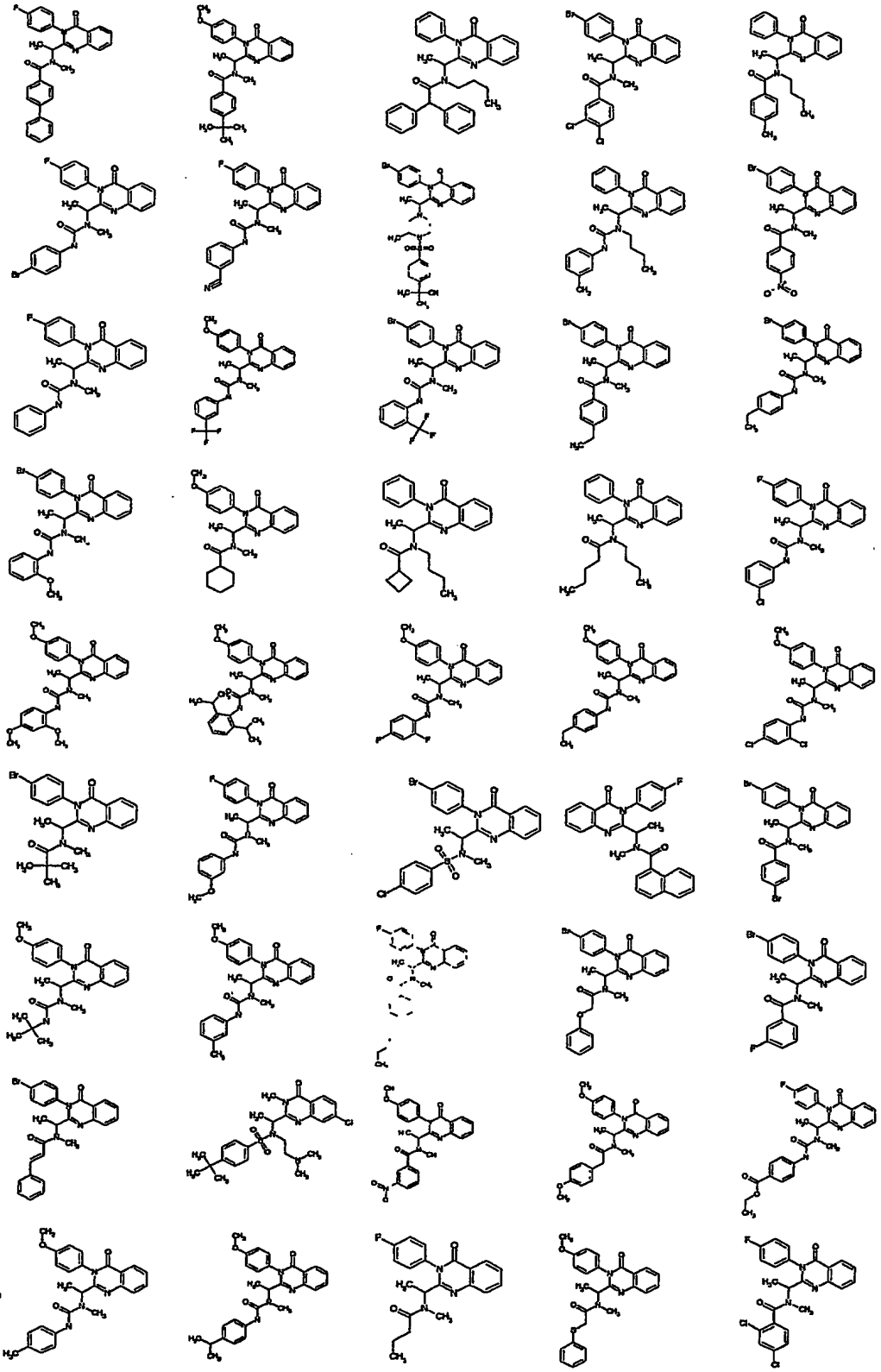

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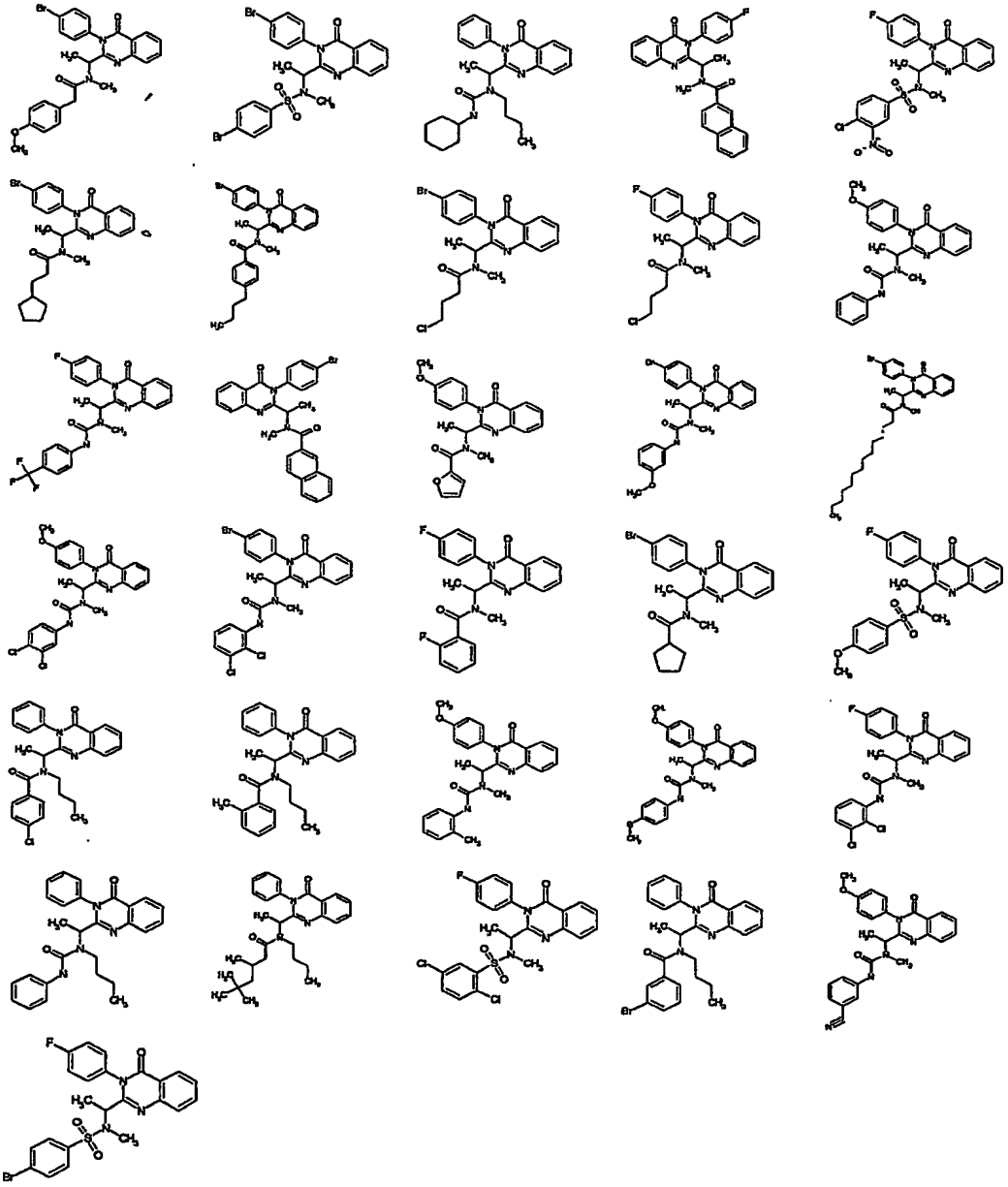

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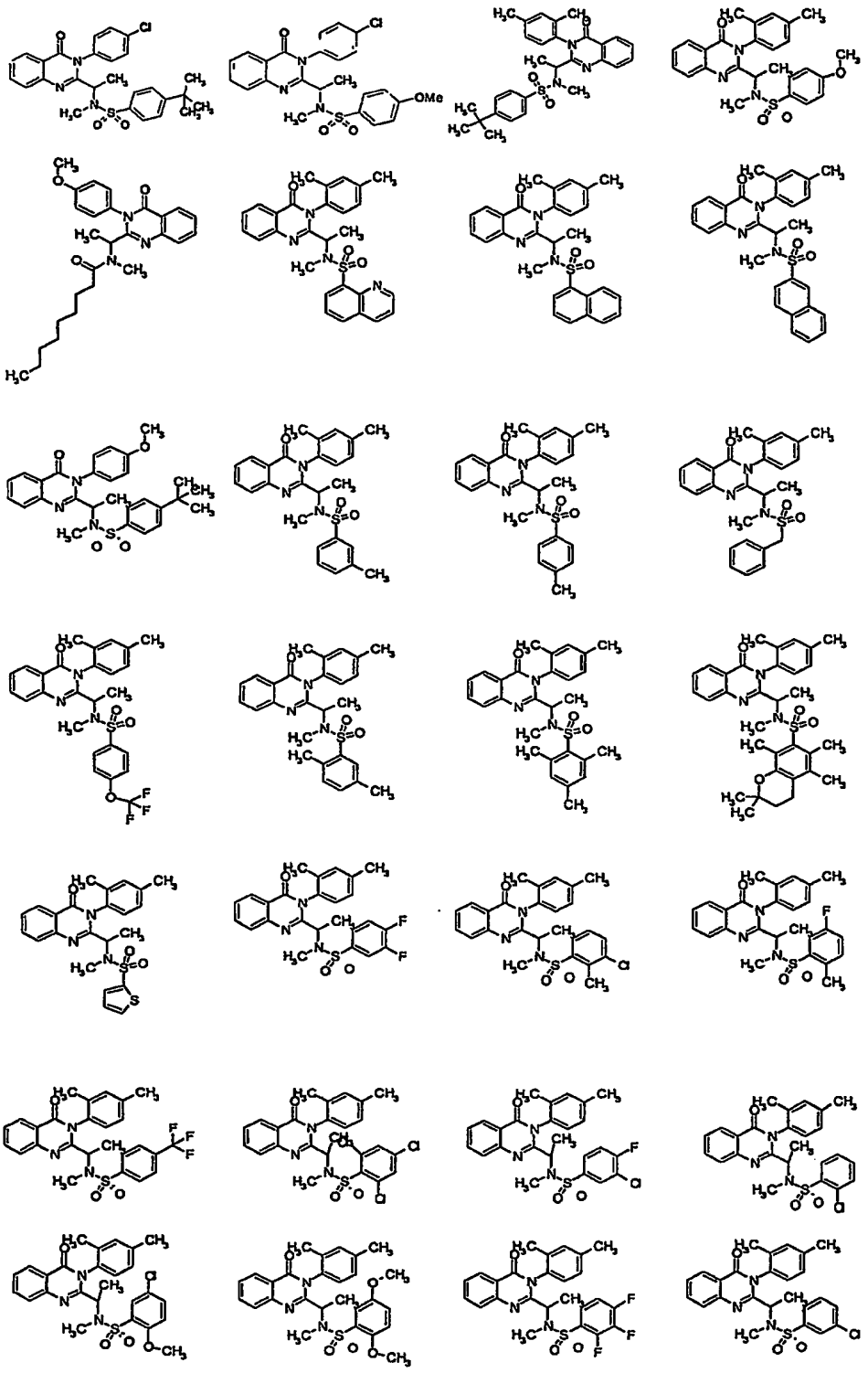

Figure 2

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Filed: March 7, 2002
Atty. Docket No.: 38205-P3002

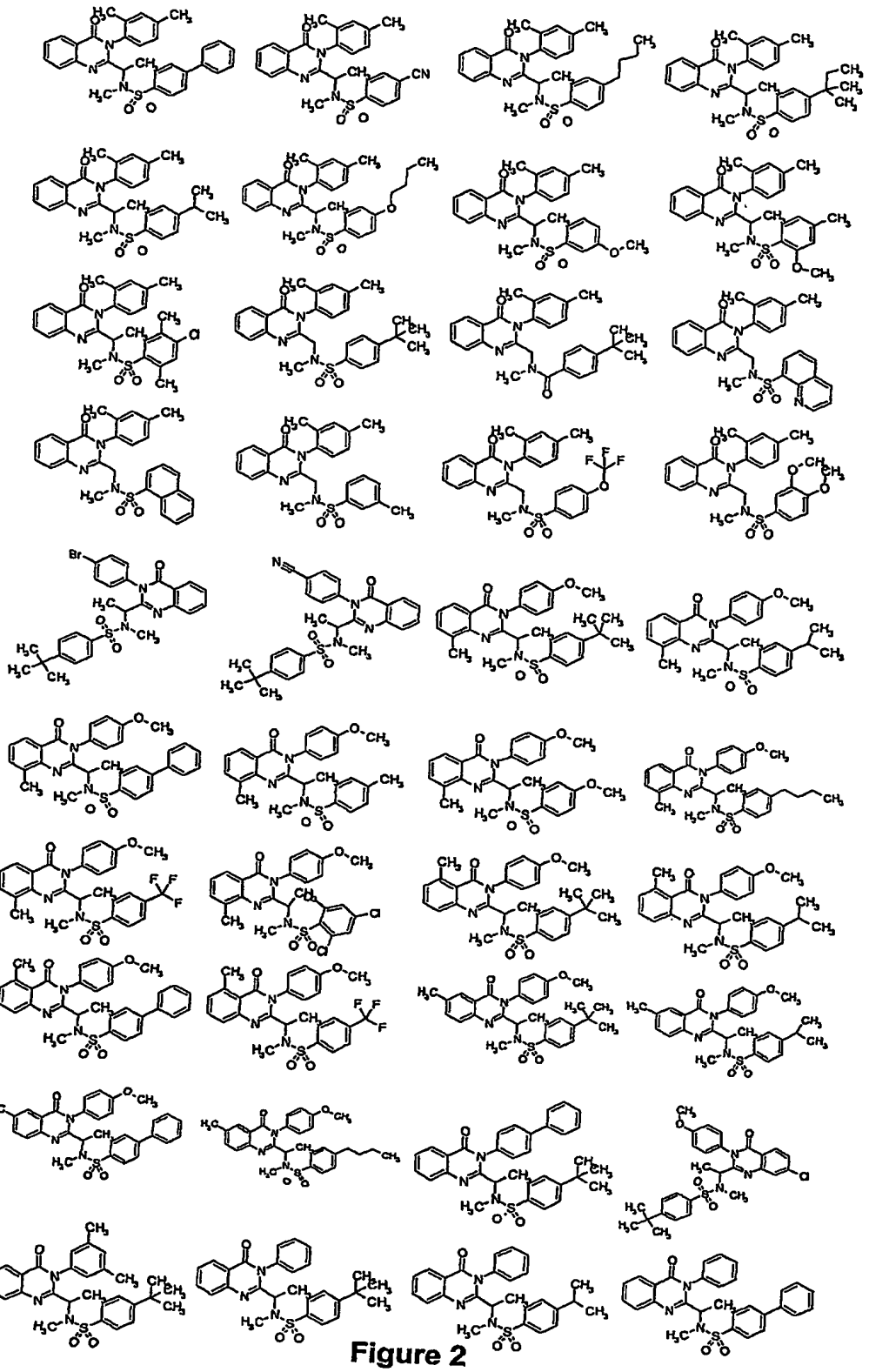

Figure 2

Applicants: Martin *et al.*
Title: QUINAZOLINONE ODULATORS OF NUCLEAR RECEPTORS
Filed: March 7, 2002
Atty Docket No.: 38205-P3002

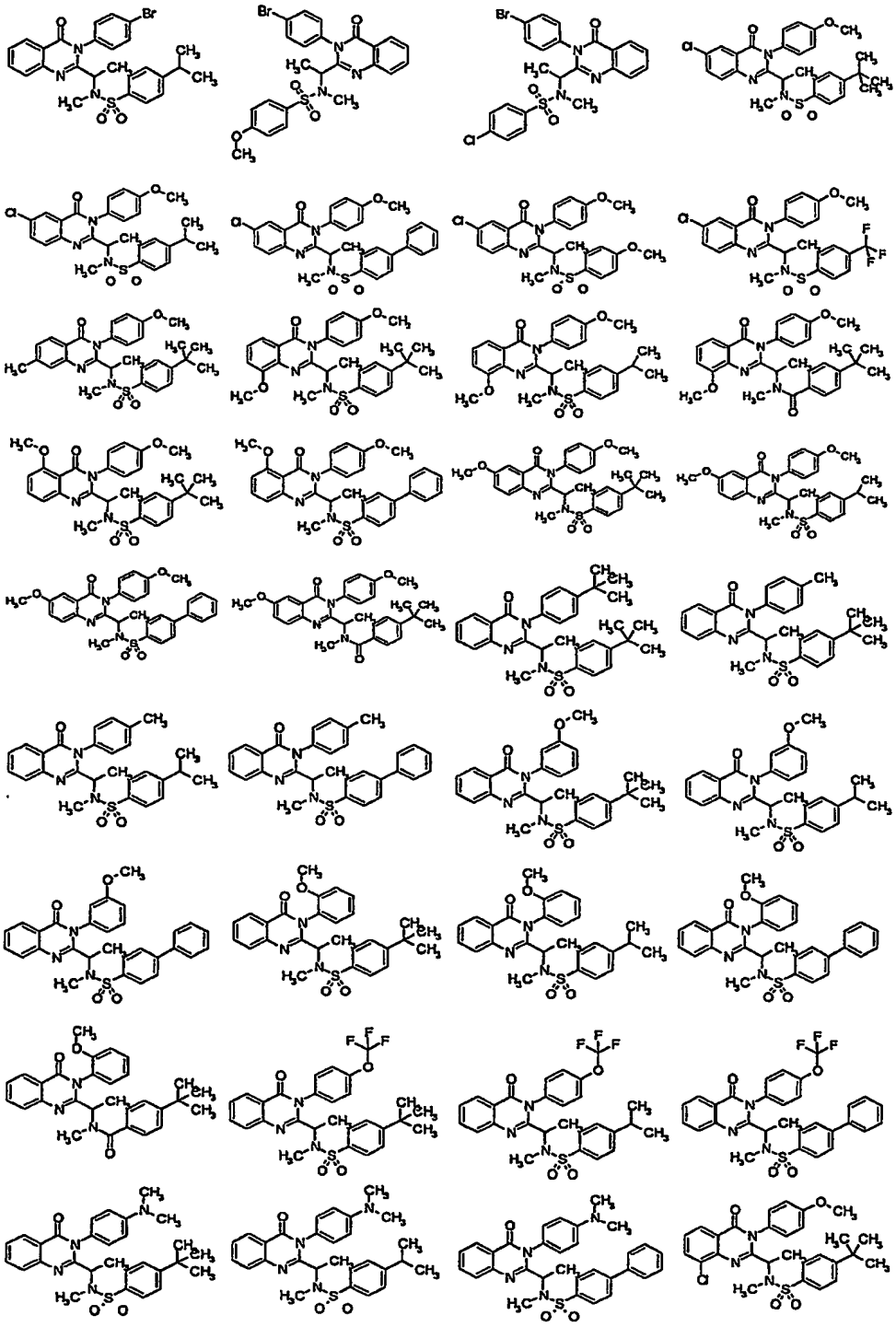

Figure 2

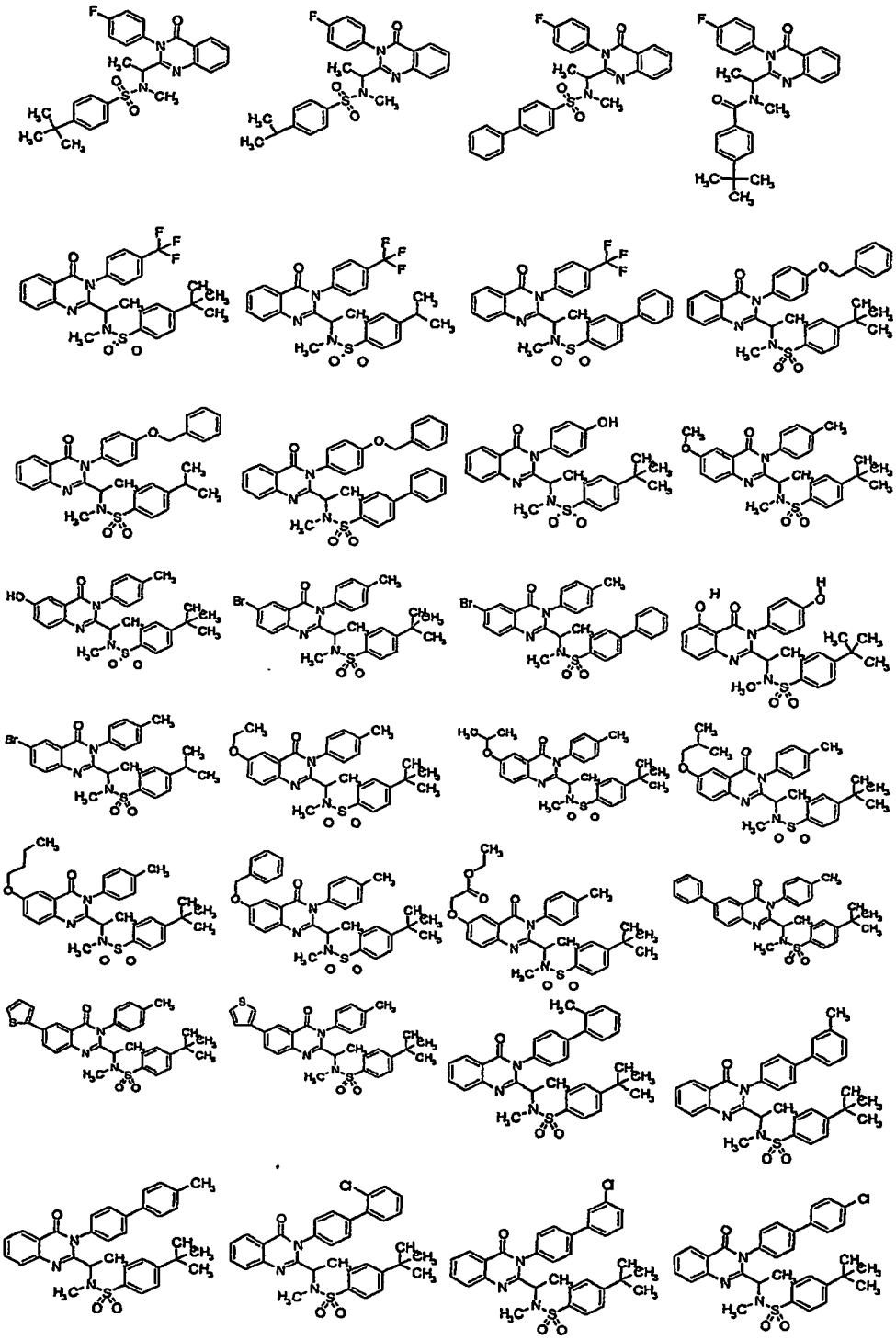

Figure 2

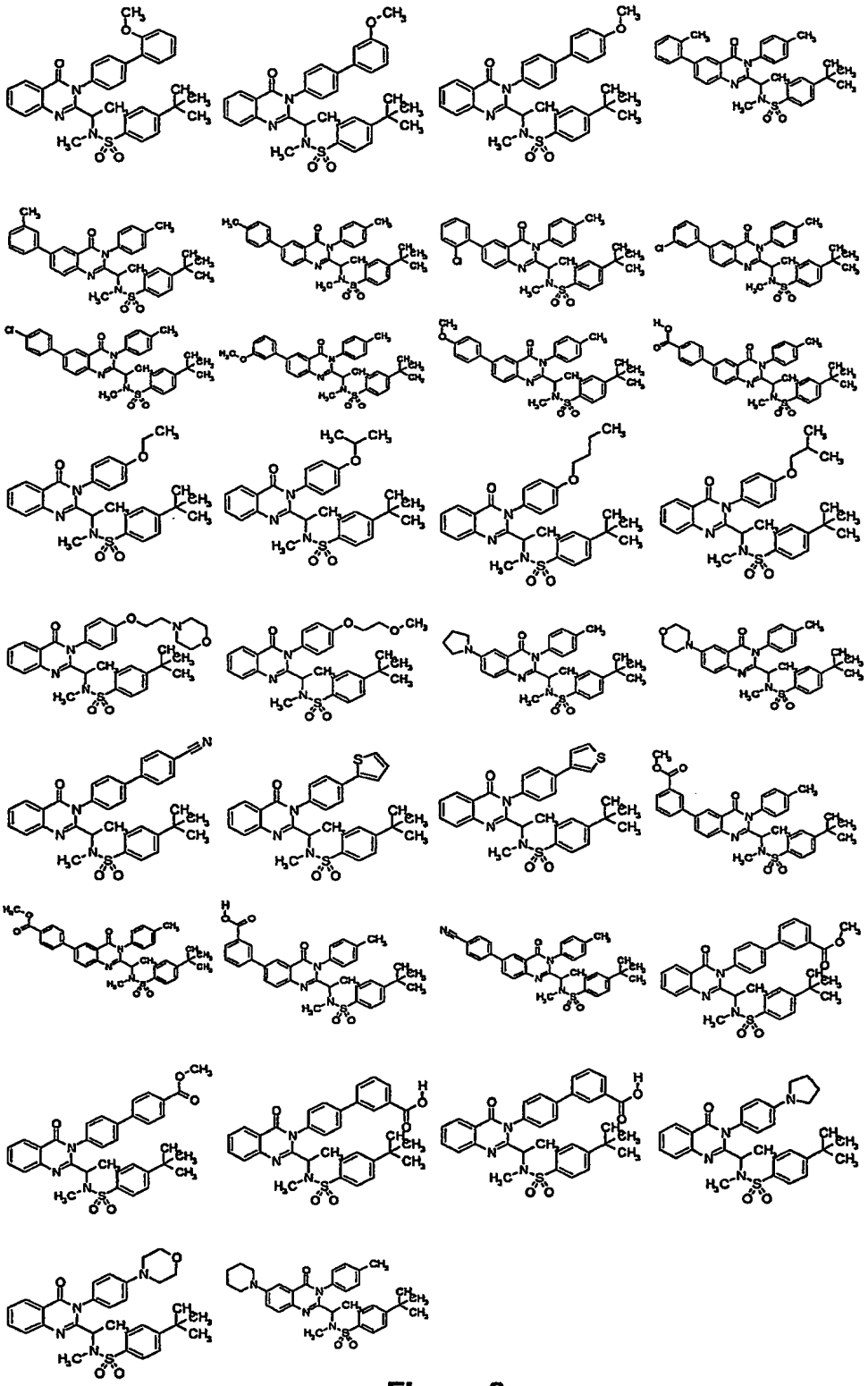

Figure 2

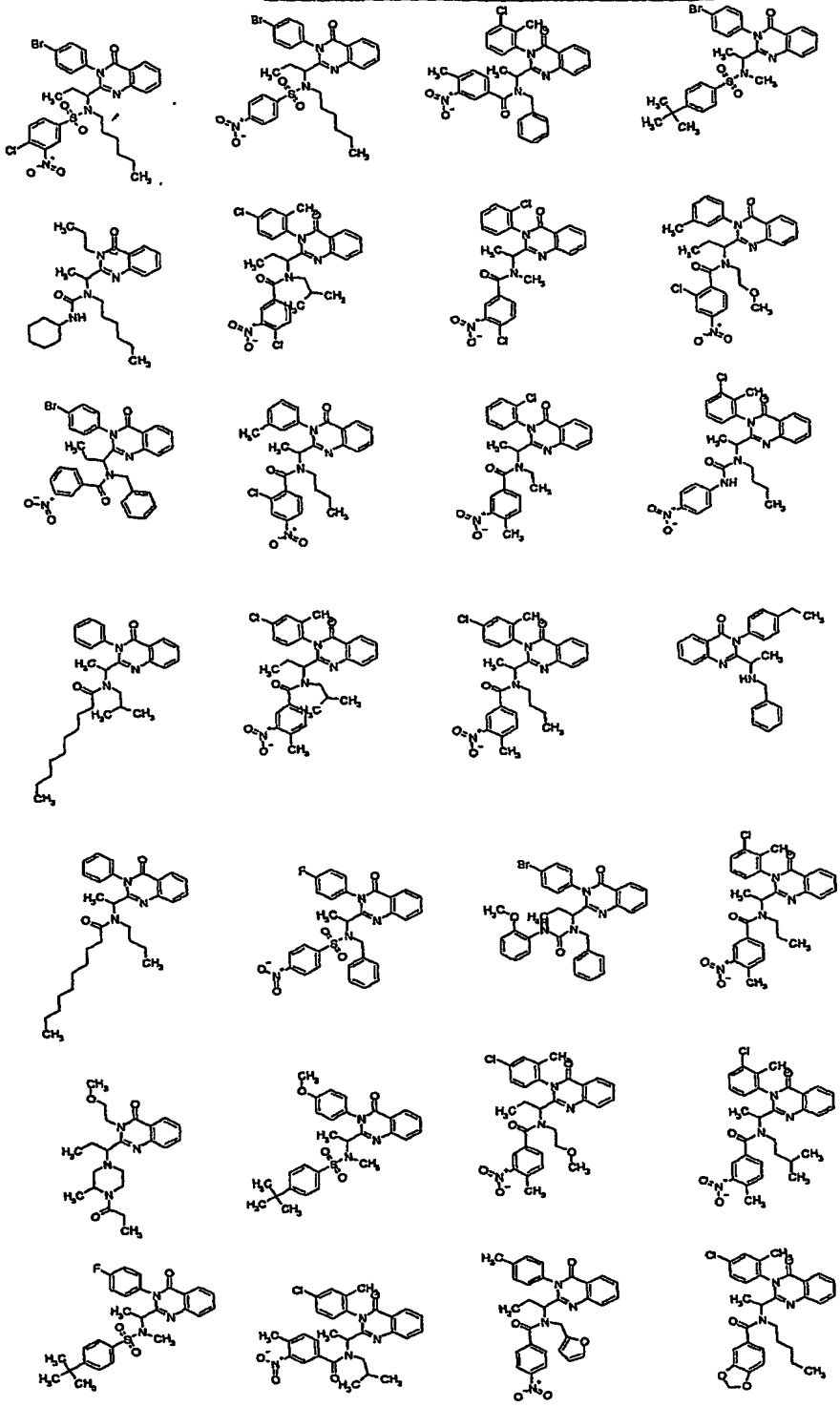

Figure 3

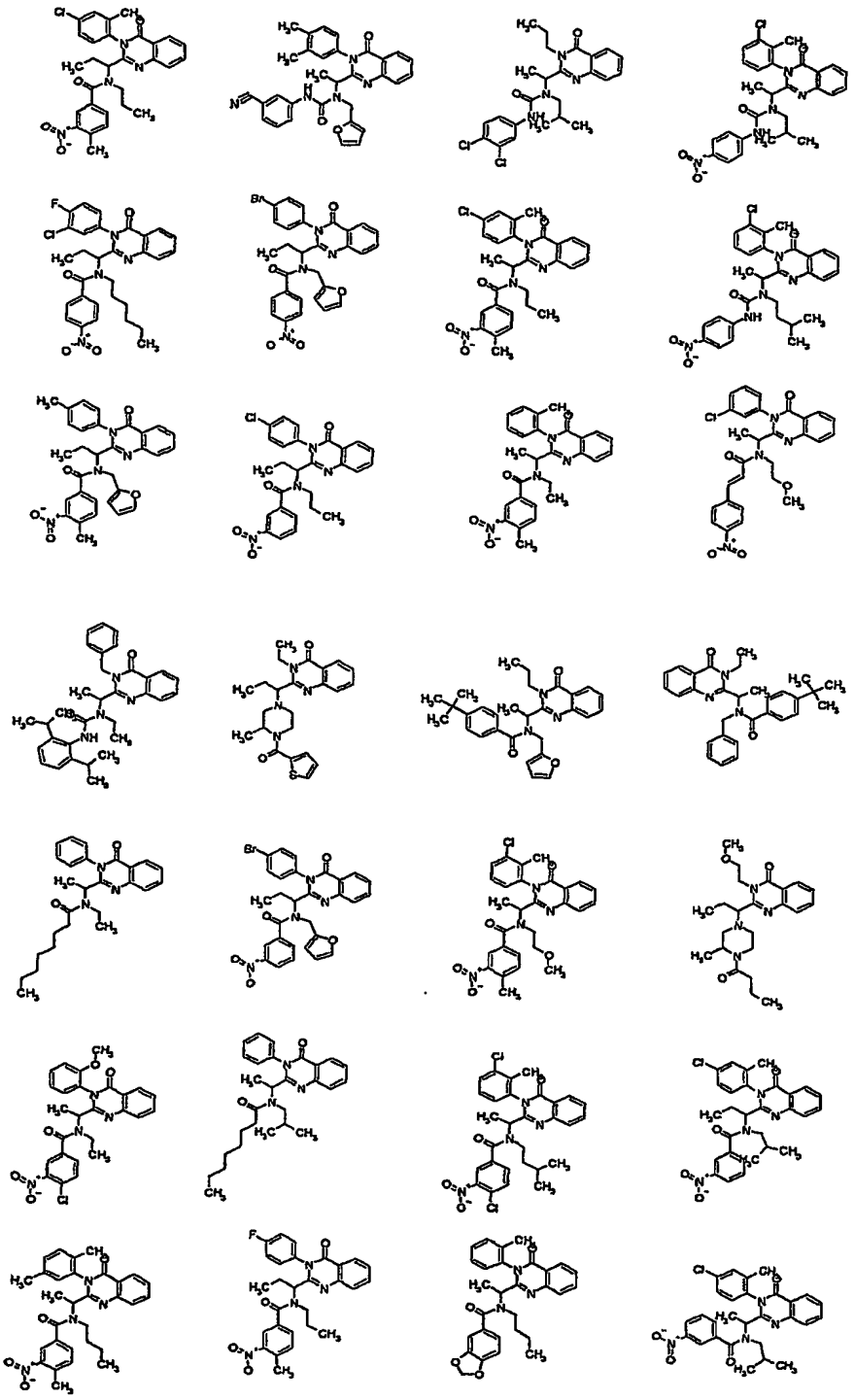

Figure 3

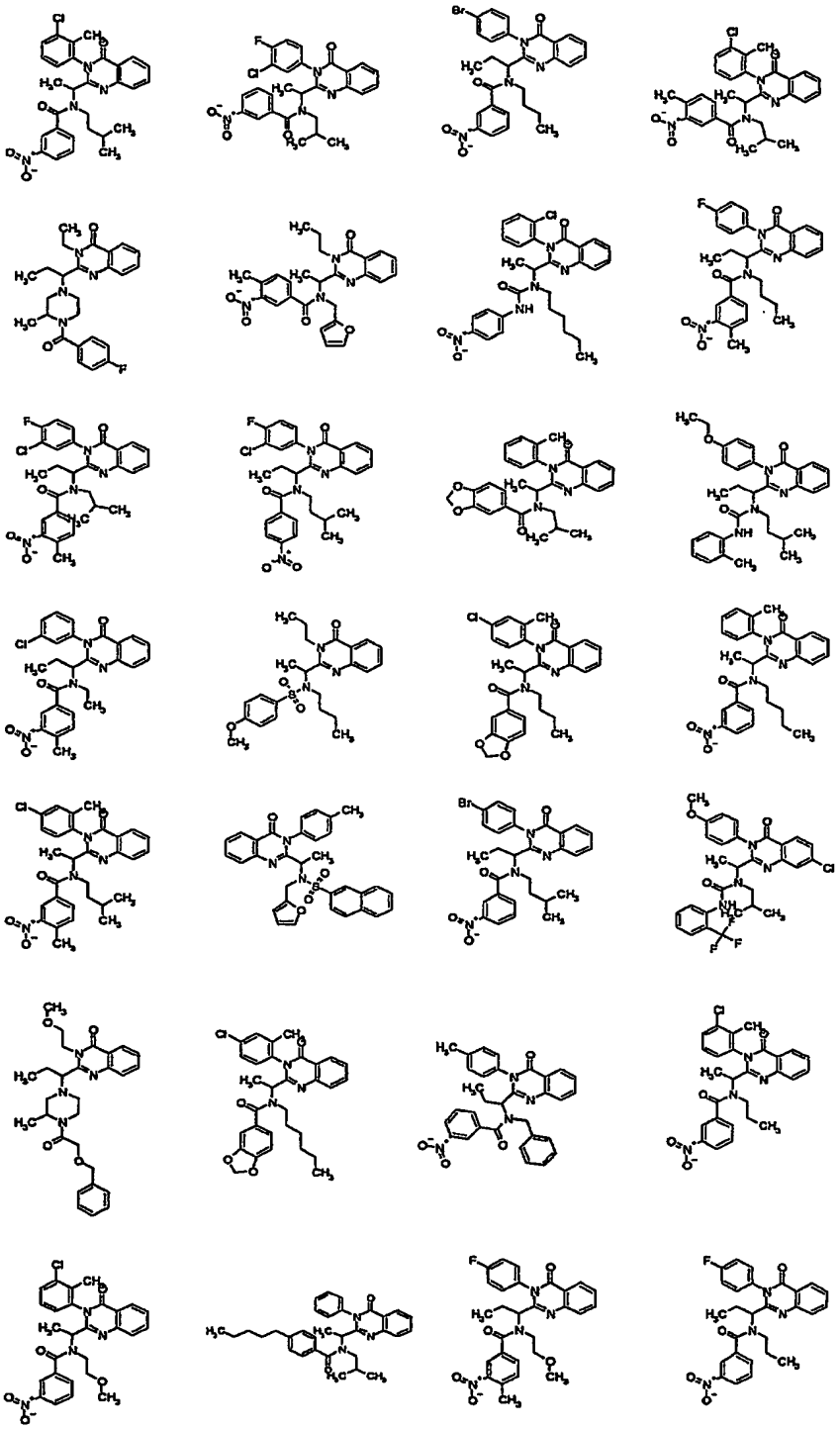

Figure 3

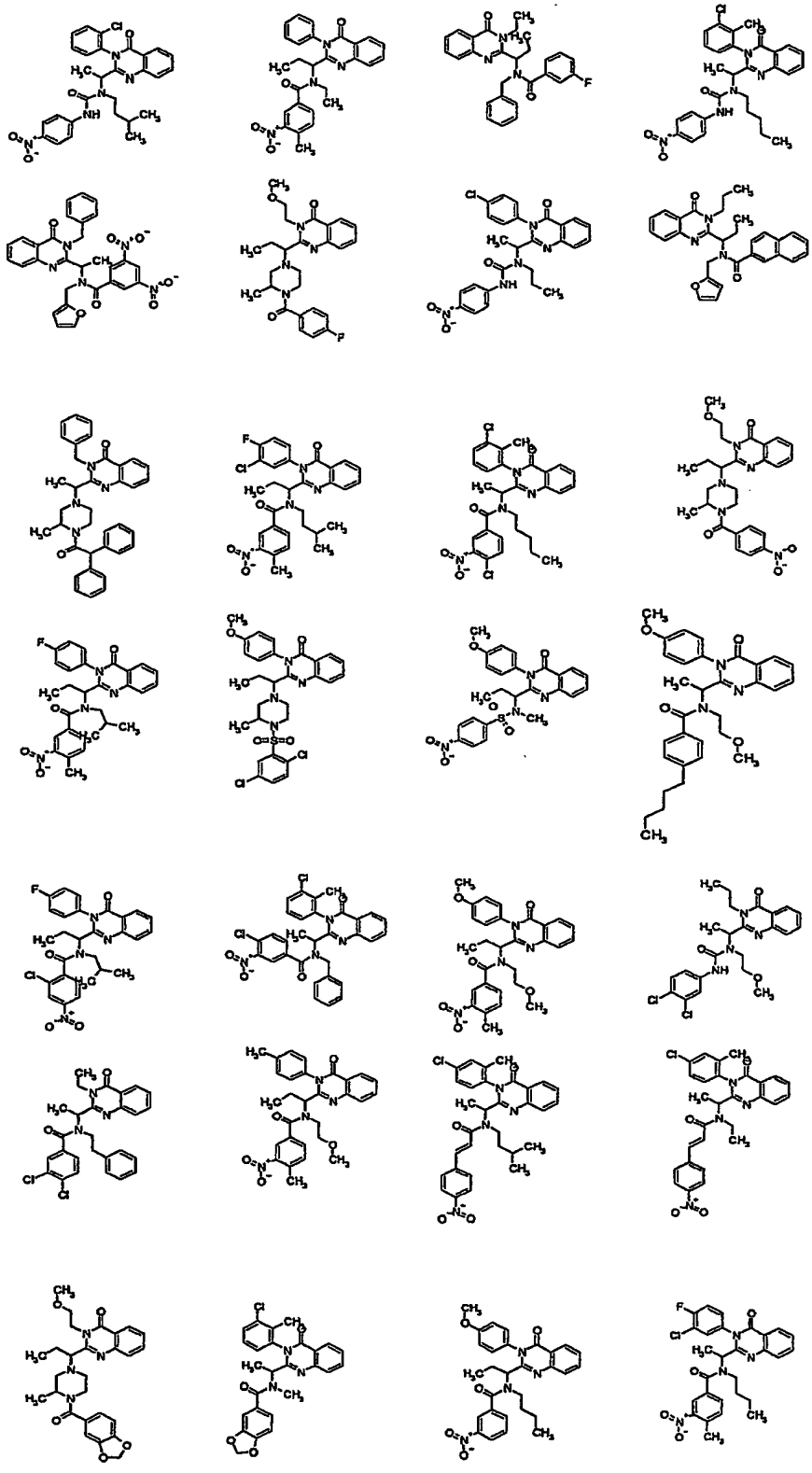

Figure 3

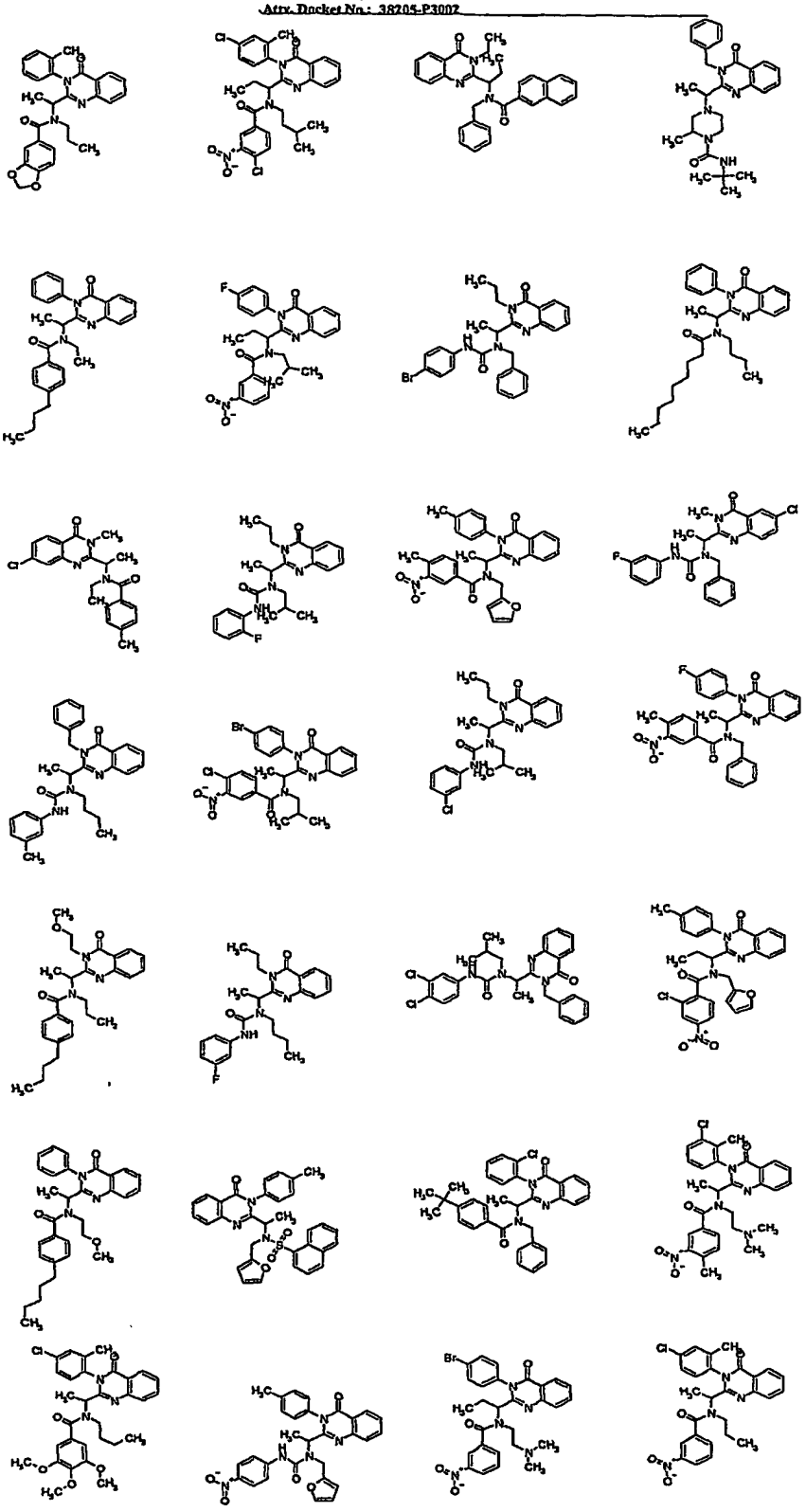

Figure 3

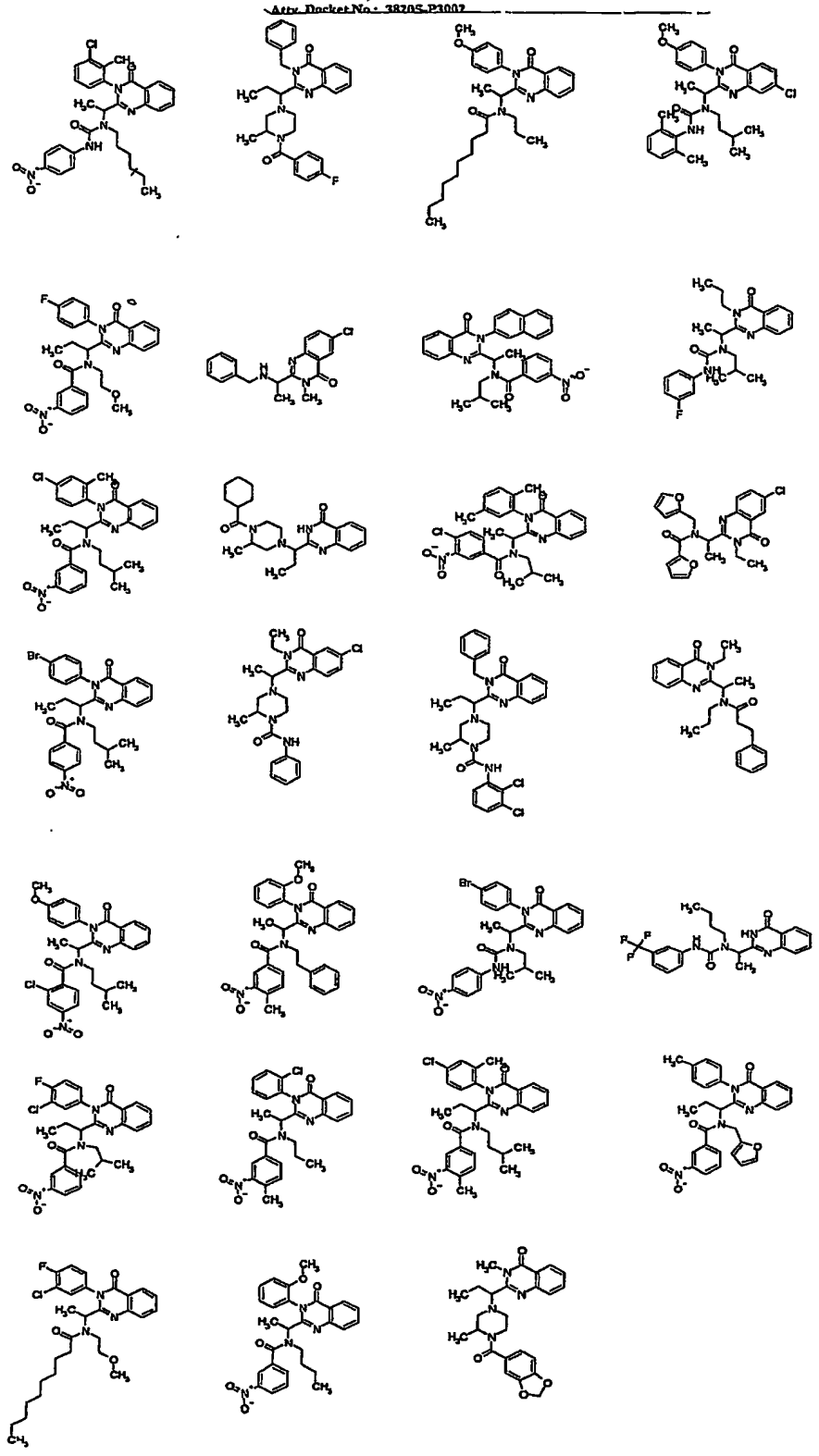

Figure 3